Docket Number EPA-HQ-OPP-2013-0524
www.regulations.gov

ortho-Phenyl Phenol (*o*PP) and Salts Final Work Plan

Registration Review: Initial Docket
Case Number 2575

March 2014

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1 Introduction

This document is the United States Environmental Protection Agency's (USEPA, EPA or "the Agency") Final Work Plan (FWP) for *ortho*-phenyl phenol (*o*PP) and its salts. The FWP document explains what EPA's Office of Pesticide Programs (OPP) knows about *o*PP and its salts, highlighting anticipated data and assessment needs, identifying the types of information that would be especially useful to the Agency in conducting the review, and providing an anticipated timeline for completing *o*PP's review.

The registration review process was designed to include a public participation component to solicit input from interested stakeholders. The Agency intends, by sharing this information in the docket, to inform the public of what it knows about oPP and its salts and what types of new data or other information would be helpful for the Agency to receive as it moves toward a decision on *o*PP and its salts.

1.1 Statutory and Regulatory Authority

The Food Quality Protection Act (FQPA) of 1996 mandated a registration review program. All pesticides distributed or sold in the United States generally must be registered by the USEPA based on scientific data showing that they will not cause unreasonable risks to human health or the environment when used as directed on product labeling. The registration review program is intended to make sure that, as the ability to assess risk evolves and as policies and practices change, all registered pesticides continue to meet the statutory standard of no unreasonable adverse effects to human health or the environment. Changes in science, public policy, and pesticide use practices will occur over time. Through the registration review program, the Agency periodically reevaluates pesticides to make sure that as change occurs, products in the marketplace can be used safely. Information on this program is provided at http://www.epa.gov/oppsrrd1/registration_review/.

The Agency is implementing the registration review program pursuant to Section 3(g) of the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA) and will review each registered pesticide every 15 years to determine whether it continues to meet the FIFRA standard for registration. The regulations governing registration review begin at 40 CFR 155.40. The Agency will consider benefits information and data as required by FIFRA. The public phase of registration review begins when the initial docket is opened for each case. The docket is the Agency's opportunity to state what it knows about the pesticide and what additional risk analyses and data or information it believes are needed to make a registration review decision.

The for *ortho*-phenyl phenol Preliminary Work Plan (PWP) was published on September 25, 2013 and the 60- day comment period ended on November 25, 2013. Public comments received concerning the PWP and documents associated with this registration review can be viewed at http://www.regulations.gov in docket EPA-HQ-OPP-2013-0524. Below is a summary of the issues relevant to this registration review case.

1.2 Updates to the Workplan

Since the publication of the PWP, the Agency has made the following updates:

- Corrected the timeline in Table 2, the anticipated registration review table.
- Updated Section 7, Next Steps.
- Added Appendix F.

The Agency received two submissions during the public comment period on the initial docket. See Appendix F for the Agency's responses to these comments.

Comments received did not result in a modification to the anticipated data needs or registration review schedule in the *o*PP PWP. This document makes final the work plan for the *o*PP and salts registration review process.

Table 1 – Summary of Anticipated Risk Assessments and Data Needs for *o*PP and its Salts

Risk Assessment	Assessment Necessary to Support Registration Review	Date of Most Recent Assessment	Type of Assessment Required	Data Anticipated as Needed (See Table 8 for details)
Dietary (food)	Yes	7/28/2006	Updated	None
Dietary (drinking water)	No (see 3.2.3)	7/28/2006	None	None
Occupational Handler (Dermal and Inhalation Exposure)	Yes	7/28/2006	Updated	Dermal and Inhalation Exposure Data
Residential Handler (Dermal and Inhalation Exposure)	Yes	7/28/2006	Updated	Dermal and Inhalation Exposure Data
Residential Post Application, Disinfected Floors (Incidental Oral Exposure)	Yes	7/28/2006	Updated	Surface Residue Data
Residential Post Application, Treated Paints (Inhalation Exposure)	Yes	7/28/2006	Updated	Paint Chamber Emissions Data
Residential Post Application, Air Sanitization (Inhalation Exposure)	Yes	7/28/2006	Updated	Inhalation Exposure Data
Residential Post Application, Treated Plastics and Polymers (Incidental Oral Exposure)	Yes	None	New	Residue Migration Data
Aggregate	Yes	7/28/2006	New	None
Cumulative	No (see 3.4.2)	7/28/2006	None	None
Tolerance Review	Yes	N/A	Updated	None
Ecological	Yes	2007	Updated	Ecotoxicity and Environmental Fate data

Table 2 – Anticipated Registration Review Schedule

Anticipated Activity	Target Date*	Completion Date
Phase 1: Opening the Docket		
Open Docket and 60-Day Comment Period for Preliminary Work Plan	2013-09	2013-09-25
Close Public Comment Period	2013-11	2013-11-25
Phase 2: Case Development		
Issue Final Work Plan	2014-03	2014-03
Issue Data Call-In (DCI)	2015-03	
Receive Data to be Considered in Risk Assessment	2017-03	
Open 30-Day Public Comment Period for Preliminary Risk Assessment(s)	2018-09	
Close Public Comment Period	2018-10	
Phase 3: Registration Review Decision and Implementation		
Open 60-Day Public Comment Period for Proposed Decision	2019-03	
Close Public Comment Period	2019-05	
Issue Final Decision	2019-09	
Begin Post-Decision Follow-up	2019	
Total (years)	6	

*The anticipated schedule will be revised as necessary (e.g., need arising under the Endocrine Disruptor Screening Program with respect to the active ingredients in this case).

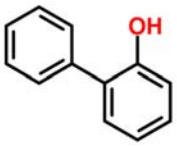
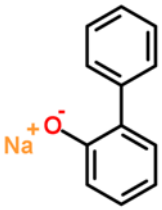
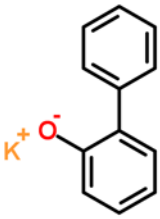
1.3 Case Overview

The docket for the *o*PP and its salts case (Case 2575) has been established at http://www.regulations.gov in docket number EPA-HQ-OPP-2013-0524.

1.4 Chemical Identification and Properties

Table 3 presents the active ingredients to be assessed in Case 2575: *ortho*-phenyl phenol (*o*PP) (PC Code 064103); sodium *ortho*-phenyl phenate a sodium salt of *o*PP (Na-*o*PP; PC Code 064104); and potassium *ortho*-phenyl phenate a potassium salt of *o*PP (K-*o*PP; PC Code 064108).

Table 3 – Chemical Identification of *o*PP and its Salts

Chemical Name	*o*PP	Na-*o*PP	K-*o*PP
Common Name	*ortho*-phenyl phenol; 2-phenyl phenol	Sodium *ortho*-phenyl phenate; *o*PP, sodium salt	Potassium *ortho*-phenyl phenate; *o*PP, potassium salt
Chemical Classification	Phenol	Phenol	Phenol
PC Code	064103	064104	064108
CAS Number	90-43-7	132-27-4	13707-65-8
Molecular Formula	$C_{12}H_{10}O$	$C_{12}H_9NaO$	$C_{12}H_9KO$
Molecular Weight	170.2 g/mole	192.19 g/mole	208.30 g/mole
Molecular Structure			

Product chemistry and fate property information relevant to the risk assessment of *o*PP and its salts is summarized in Table 4. Details of the fate properties are included in Appendix B and details of the product chemistry information are included in Appendix E . In solution, the sodium (Na) and potassium (K) salts rapidly dissociate, releasing sodium and potassium cations (Na^+ and K^+, respectively) and the *ortho*-phenyl phenate anion (oPP^-). The equilibrium in solution between the oPP^- anion and the protonated or unionized *o*PP depends on the pH of the solution. The fate and transport data supporting *o*PP can be used to support the salts, and similarly, the fate and transport data supporting its Na and K salts may be used to support *o*PP.

Table 4 – Physical-Chemical and Fate Properties for *o*PP and its Salts

OPPTS Guideline No.	Physical and Chemical Properties	*o*PP	Na-*o*PP	K-*o*PP
830.7000	pH	6.1 in aqueous solution at 22.7°C	12 to 13.5 in saturated water solution at 25°C	12 to 13.5 in saturated water solution at 25°C
830.7050	UV/Visible Absorption	245 to 287nm Not expected to absorb UV at λ > 300 nm	--	--
830.7200	Melting point	56-58°C	230.07°C (Source: EPI Suite v4.1)	230.07°C (Source: EPI Suite v4.1)

OPPTS Guideline No.	Physical and Chemical Properties	*o*PP	Na-*o*PP	K-*o*PP
830.7220	Boiling point	286ºC at 760 mm Hg	537.41°C (Source: EPI Suite v4.1)	537.41°C (Source: EPI Suite v4.1)
830.7300	Density	1.213 g/cu cm at 25°C	1.3 g/cu cm at 25°C	1.3 g/cu cm at 25°C
830.7370	Dissociation Constants in water	pKa = 9.55 at 22.5°C pKa = 9.9 at 25°C pKa = 9.97 at 25°C It is a weak acid.	Dissociates in water pKa: 9.84 at 20ºC	Dissociates in water pKa: 9.84 at 20ºC
830.7550	Partition coefficient (*n*-octanol/water) Log *K*ow	3.3 (EPI Suite v4.1) log Pow: 3.09-3.36 log Pow: 3.12 (20°C, pH 7)	0.59 (EPI Suite v4.1)	0.59 (EPI Suite v4.1)
830.7840	Water Solubility	700 mg/L at 25°C in water 0.760 g/1000 g in water (pH 5.67) (20ºC).	60.6 g/100 mL, 53.37% (w/w) (20ºC) 534 g/1000 g in water (pH 13.61) (20ºC)	Highly water soluble 534 g/1000 g in water (pH 13.61) (20ºC)
830.7950	Vapor pressure	2.00 x 10^{-3} mm Hg at 25°C (EPI Suite v4.1, experimental) 1.6 x 10^{-3} mm Hg at 25ºC 0.0017 mmHg at 25ºC	1.91 x 10^{-11} mm Hg at 25 °C (Source: EPI Suite v4.1) 1.8 x 10^{-9} mm Hg at 25ºC	1.91 x 10^{-11} mm Hg at 25 °C (EPI Suite v4.1)

Source: MRIDs 101697, 41914901, 41605001, 41609501, 41609502, 41609503, 41609504, 41609505, 42097001, 42381901, 42441701, 42441702, 42441703, 42441704, 42457001, 42500201, 42500202, 42528701, and 43994201, EPI Suite v4.1

1.5 Use/Usage Description

1.5.1 Summary of Registered Uses

Table 5 includes a summary of end use products that contain *o*PP or its salts as an active ingredient (a.i.).

Table 5 – Summary of End Use Products Containing *o*PP or its Salts

Chemical Name	PC Code	Number of Products	Percent a.i.	Formulations
*o*PP	064103	77	0.014 to 99.5	Pressurized Liquid, Soluble Concentrate (SC), Ready to Use (RTU) Solution, Wipe
Na-*o*PP	064104	19	0.21 to 71.7	SC, RTU Solution, Emulsifiable Concentrate, Pressurized Liquid (i.e., aerosol can)
K-*o*PP	064108	3	0.159 to 55.6	SC, Pressurized Liquid

Table 6 includes a summary of the registered *o*PP and salts uses that will be assessed in this registration review. Registered product uses include: disinfectants, bacteriocides/bacteriostats, deodorizers, algaecides, fungicides/fungistats, insecticides, miticides, molluscicides, sanitizers, termiticides, tuberculocides, and virucides.

Table 6 – Summary of Registered Uses of *o*PP and its Salts

Use	Application Method	Application Rate
Agricultural Premises and Equipment		
Greenhouse premises and equipment	Sponge, Mop, Spray	233 to 268 ppm
Cattle, Swine and Poultry Farms Hatching facilities and incubators Trucks and other vehicles	Sponge, Mop, Spray RTU Spray	194 to 782 ppm 2,200 ppm
	Fogger	3,200 to 40,350 ppm in fogging solution
Shoe sanitizer	Shoe Bath Tray	233 to 476 ppm
Aquatic Areas		
Sewage Disposal Lagoons[1]	Spray	4 lb ai/acre
Commercial/Institutional/Industrial (CII) Premises and Equipment		
Nonporous, nonfood contact surfaces including transportation facilities and vehicles, storage facilities, and general indoor premises.	Sponge/Mop/Spray RTU Spray	233 to 782 ppm 140 to 4,000 ppm
	Fogger	3,200 to 40,350 ppm in fogging solution
Utility pole junction boxes[2]	RTU Spray	2,100 ppm
Post-Harvest Fruit Treatment and Wash		
Post-harvest fruit treatments and Fruit washes (Citrus, Peach, Pear)[3]	Drench, Dip, Drip, Spray, Foam	3593 to 134,000 ppm 359 to 4,300 ppm 3,600 to 15,600 ppm
Food Handling Premises and Equipment		
Food processing plants; non-food handling areas	Spray (RTU)	500 to 2,200 ppm
	Sponge, Mop	258 to 2,200 ppm
Eating establishment food handling areas	Spray (RTU)	500 to 2,200 ppm
	Sponge, Mop	158 to 410 ppm
Industrial Processes		
Air Washer, Cooling Tower and Paper Mill Water Systems	Open Pour	6.2 to 12.4 ppm
Oil Drilling Muds, Packer Fluids, Oil field water systems, Oil Recovery Water, Secondary	Open Pour	86 to 4,300 ppm 6.2 to 12.4 ppm
Material Preservative		
Adhesives, Glues, Caulks and Sealants	Open Pour	500 to 11,400 ppm
Ceramic glazes	Open Pour	375 to 5,600 ppm
Cleaning Solutions	Open Pour	375 to 4,600 ppm
Vehicle polishes and waxes	Open Pour	625 to 5040 ppm
Concrete and Concrete Additives	Open Pour	875 to 7,170 ppm
Leather	Dip and Spray	690 to 15,000 ppm

[1] The Sewage Disposal Lagoons use is included on EPA Reg # 39967-116.
[2] The Utility pole junction boxes use is included on EPA Reg # 9688-287.
[3] Per Tolerances in 40 CFR 180.129.

Use	Application Method	Application Rate
Metal Working Fluids	Open Pour	500 to 15000 ppm
Paints, Stains and Coatings (In Can)[4] Finger Paint[5]	Open Pour	500 to 5,700 ppm
Paper Auxillaries and Additives	Open Pour	400 to– 4300 ppm
Plastics	Open Pour	5000 ppm
Polymer Dispersions and Emulsions (i.e. rubber)	Open Pour	500 to 3,800 ppm
Textile Auxillaries	Open Pour	500 to 4,300 ppm
Textiles (Awnings and Tarps) Textiles (Carpet and Upholstery) Textiles (Cotton)	Open Pour	8,700 to 56,600 ppm 3,500 to 22,600 ppm 2,600 to 17,000 ppm
Medical Premises and Equipment		
Critical Items (Surgical Equipment)	Immersion	84 to 536 ppm
Hair Care Shavers and Scissors	Immersion	22 to 782 ppm
Dental Lines	Circulate in Place	268 to 537 ppm
Hard Surfaces (Noncritical Areas) Hard Surfaces (Critical Areas)	Mop, Wipe, Spray	196 to 1,550 ppm 196 to 520 ppm
Residential and Public Access Premises		
Hard surfaces including floors and bathrooms	Sponge, Mop or Spray RTU Spray	194 to 1,550 ppm 500 to 3,700 ppm
Exterior roof, siding, trim, decks, fences	Spray	118 ppm acid equivalents (20 gallons per 2,000 ft^2 roof and 20 gallons ft^2 other structures
Carpets and Upholstery	RTU Spray	2,200 ppm
Bedding and Mattresses	RTU Spray	1,800 to 2,200 ppm
Laundry and Footwear	RTU Spray	1,000 to 2,200 ppm
Portable Toilets	Open Pour	409 to 288,000 ppm
Garbage Cans	Spray RTU Spray	258 to 520 ppm 140 to 4,000 ppm
Wood Preservative including Sapstain Control		
Fresh Cut Lumber, Construction Woods Fruit and Vegetable Containers, Pallets	Dip or Spray	6,870 to 45,200 ppm 32,000 to 34,000 ppm
Residential Lawn, Turf, and Surface Treatments		
Lawn, turf, outdoor soil and plant beds and vegetation adjacent to building foundations and structures including decks, porches, and fences; sidewalks, driveways, patios, and porches; ant hills	Spray including spot treatments and crack-in-crevice treatments	Up to 0.133 lb a.i./A [6]

[4] The "In Can" designation refers to the a.i. added to preserve the material in the container prior to in-service use.
[5] The finger paint use is included on EPA Reg # 39967-188.
[6] This application rate assumes 4 houses per acre (quarter-acre lot per house) and that each homeowner applies the entire contents of one container of spray (=170 ounces). Therefore, the application rate in pounds a.i. per acre (lb a.i./A) is 0.133 (4 houses per acre x 1 container per house x 170 ounces per container x 1 gallon per 128 ounces (unit conversion) x 8.33 lb/gallon (density for water) x 0.003 (% a.i.)).

1.6 Regulatory History

The first product containing *o*PP as an a.i. was registered in the U.S. in 1948. The first product containing Na-*o*PP as an active ingredient was registered in the U.S. in 1948. The first product containing K-*o*PP as an active ingredient was registered in the U.S. in 1996. The Agency completed a Reregistration Eligibility Decision (RED) for the *o*PP and its salts case in 2006. The post-RED Data Call-In (DCI) has not been issued.

1.6.1 Recent/Pending Regulatory Actions

An EDSP order for submission of *o*PP data was issued on January 14, 2010. Data have been submitted and are currently being reviewed.

1.7 Incidents

1.7.1 Human Health

Incidents Reported in the OPP Incident Data System

As of July 9, 2013, a total of 1147 human health incidents that have occurred since the 2006 RED was published are listed in the Office of Pesticides Programs Incident System for *o*PP and its salts. Most (855) of these incidents involved dual purpose products that contain disinfectants and insecticides such as cyfluthrin, permethrin, and pyrethrin while a smaller number of incidents were associated with disinfectant only products. A listing of these incidents is given in Table **7**.

Table 7 - Incidents Reported for *o*PP and its Salts (July 2006 to July 2013)

Product Type	Number of Incidents					
	Fatality	Major	Moderate	Minor	Unclassified	Total
Disinfectant-Only	1	2	45	172	12	232
Insecticide/Disinfectant (Cyfluthrin)	0	1	73	781	0	855
Insecticide/Disinfectant (Pyrethrin)	0	0	11	49	0	60
Total	1	3	129	1002	12	1147

Most of the incidents are classified as Minor (1002 incidents) while a smaller number are classified as Moderate (129 incidents), Major (3 incidents) and Fatality (1 incident). The circumstances surrounding the fatality and the three major incidents are as follows:

- The fatality involved a baby who was born six weeks early with excessive fluid in the abdomen. The mother used a product containing *o*PP on a regular basis while she was pregnant.
- One of the disinfectant-only major incidents involved a man who had been using the product without gloves, who was hospitalized with acute pancreatitis and secondary respiratory failure.
- The other disinfectant-only major incidents involved an employee who suffered respiratory arrest after being exposed to the product.
- The disinfectant/insecticide major incident involved a person who had an intraventricular hemorrhage sometime shortly after spraying the product.

With respect to the above incidents, the fact that they are listed in the incident data system does not necessarily mean that they were caused by the associated product. In the case of the intraventricular hemorrhage, for example, the emergency medical technicians on the scene

reported the presence of the product to aide in diagnosis, and it was later determined by the doctors at the hospital that the hemorrhage was not caused by the product.

The moderate incidents involved a wide range of circumstances and effects. Some of the incidents were caused by misuse of the product on unregistered use sites such a toilet seats or over use of the product where too much product was applied or the product was applied too often. The reported effects included dermal irritation and hives, respiratory irritation and systemic effects such as dizziness and nausea.

1.7.2 **Ecological**

No incidents are reported in the Agency's Incident Data System (IDS v. 1.8) for the time period spanning 2006 to 2013.

2 Anticipated Data Needs

Table 8 presents a summary of the data anticipated as being needed to support this registration review.

Table 8 – Studies Anticipated as Needed for the Registration Review of *o*PP and its Salts

GLN	Study Name	Test Substance[7]	Time Frame (Measured in months from DCI Receipt)	Risk Assessment(s) Data Will Support	Use Site(s) Triggering Anticipated Data Requirement	Applicable Exposure Scenario
Studies Anticipated to be Required through the Registration Review DCI						
835.1110	Activated Sludge Sorption Isotherm	TGAI	12	Ecological	Sanitizer/Disinfectant; Materials preservatives; Antimicrobial fruit and vegetable washes; food contact sanitizer; Wood Preservative for sapstain control; Swimming pools, spas, ornamental ponds, aquaria, waterbed water; Commercial/Industrial Process and Water Systems; Biocides in oil drilling muds and secondary recovery water	Transport to wastewater treatment plants and potential subsequent exposure to aquatic organisms in surface water
835.1230	Adsorption/Desorption	TGAI	12	Ecological	Wood preservative; Exterior architectural paints and coatings material preservative; Exterior roof, siding, fence, and deck algaecide and antimicrobial treatment; Lawn, turf, surface soil, sidewalk, parking lot, patio, ant hill insecticide use	Treated wood; Exterior paint/stain; Exterior building and structure treatment; Residential lawn and impervious surface
835.1240	Leaching Studies, Soil	TGAI	12			
835.2240	Photodegradation in Water	TGAI	12	Ecological	All	Industrial processes; DtD premise and equipment uses; Material preservatives with DtD releases; Residential lawn and impervious surface; Treated wood; Exterior paint/stain; Exterior building and structure treatment; Residential lawn and impervious surface
835.2410	Photodegradation in Soil	TGAI	12	Ecological	Wood preservative; Exterior architectural paints and coatings material preservative; Exterior roof,	Leaching from treated wood; Exterior paint/stain; Leaching from Exterior building and structure

[7] The Agency lacks information on the fate profile for oPP with regard to the potential for biotic degradates/transformation products to be formed. Consequently, in the absence of information, the Agency will use a total toxic residue approach to determine potential toxicity to ecological organisms. This approach assumes any major degradates formed would be as toxic as the parent. The Agency will consider conducting a more refined risk assessment if information on toxicity of any major degradates identified is provided.

GLN	Study Name	Test Substance[7]	Time Frame (Measured in months from DCI Receipt)	Risk Assessment(s) Data Will Support	Use Site(s) Triggering Anticipated Data Requirement	Applicable Exposure Scenario
835.4100	Aerobic Soil Metabolism	TGAI	24		siding, fence, and deck algaecide and antimicrobial treatment; Lawn, turf, surface soil, sidewalk, parking lot, patio, ant hill insecticide use	treatment; Run-off to Residential lawn and impervious surface
835.4300	Aerobic Aquatic Metabolism	TGAI	24	Ecological	All	Transport to wastewater treatment plant (WWTP) and subsequent release to surface water downstream; leaching and run-off to surface water; transport to surface water via stormwater drain; direct discharge to surface water
835.4400	Anaerobic Aquatic Metabolism	TGAI	24			
OECD 209 or 850.6800[8]	Activated Sludge Respiration Inhibition (ASRI)	TGAI	12	Ecological	Sanitizer/Disinfectant; Materials preservatives; Antimicrobial fruit and vegetable washes; food contact sanitizer; Wood Preservative for sapstain control; Swimming pools, spas, ornamental ponds, aquaria, waterbed water; Commercial/Industrial Process and Water Systems; Biocides in oil drilling muds and secondary recovery water	Transport to wastewater treatment plant and potential effects to and biodegradation by WWTP microorganisms
835.3110 835.3220 835.3240 835.3280	Ready biodegradability test or one of three biodegradation in activated sludge simulation tests[9]	TGAI	12			

[8] EPA published draft guidance under guideline OPPTS 850.6800 and has since published final guidance for this study under guideline OCSPP 850.3300: http://www.regulations.gov/#!documentDetail;D=EPA-HQ-OPPT-2009-0154-0021. The anticipated DCI will provide that OCSPP 850.3300 may be used in place of OECD 209 if the test substance is not sufficiently soluble to allow preparation of a concentrated stock solution in water. The Agency has included this study in 40 CFR 158(W). OECD Test Guideline 209 can also be used as guidance for this study, available online at http://www.oecd-ilibrary.org/content/book/9789264070080-en.

[9] The results of the ASRI test will determine which of these four biodegradation tests is/are required. If the ASRI test EC_{50} is less than or equal to 20 mg/L, then either the (i)Biodegradation in Activated Sludge Study or (ii) Simulation Test – Aerobic Sewage Treatment: A. Activated Sludge Units or (iii) the Porous Pot Test is expected to be required. If the ASRI test EC_{50} is greater than 20 mg/L, then the registrant would likely be required to conduct either: (i) Ready Biodegradability or (ii) a) Biodegradation in Activated Sludge or b) Simulation Test – Aerobic Sewage Treatment: A. Activated Sludge Units or c) the Porous Pot Test. If the Ready Biodegradability study is conducted and passes, then no further testing would be expected to be required. If, however, the antimicrobial fails the Ready Biodegradability study, then the a) Biodegradation in Activated Sludge or b) Simulation Test – Aerobic Sewage Treatment: A. Activated Sludge Units, or c) the Porous Pot study would likely be required.

GLN	Study Name	Test Substance[7]	Time Frame (Measured in months from DCI Receipt)	Risk Assessment(s) Data Will Support	Use Site(s) Triggering Anticipated Data Requirement	Applicable Exposure Scenario
Special Study	Leaching study, paint, stain and coatings; concrete	TEP	24	Ecological	Material Preservative (Paints, stains, and coatings; concrete and concrete additives; ceramic glazes)	Leaching/run-off from exterior in-service use of preserved paints/stains/coatings, concrete and concrete additives
Special Study	Leaching study, cotton textiles	TEP	24	Ecological	Material Preservative Textile	Leaching and subsequent transport to soil and potential run-off to surface water; leaching from textiles via washing textiles followed by transport to wastewater treatment plants and potential subsequent transport to surface water
850.1350	Aquatic invertebrate life cycle (saltwater)	TGAI	24	Ecological	All	Transport to wastewater treatment plant (WWTP) and subsequent release to surface water downstream; leaching and run-off to surface water; transport to surface water via stormwater drain; direct discharge to surface water
Non-guideline	Whole sediment chronic toxicity[10]	TGAI	24	Ecological		
850.1710	Oyster BCF	TGAI	24	Ecological		
850.1730	Fish BCF	TGAI	24	Ecological		
850.2100	Avian oral toxicity (passerine species)	TGAI	24	Ecological	Lawn, turf, surface soil, sidewalk, parking lot, patio, ant hill insecticide use	Residential lawn and impervious surface
850.2300	Avian reproduction[11]	TGAI	24	Ecological		
850.3020	Honey bee acute contact toxicity	TGAI	12	Ecological	Wood preservative; Lawn, turf, surface soil, sidewalk, parking lot, patio, ant hill insecticide use	Treated wood
850.3030[12]	Honey bee toxicity of residues on wood	TGAI	12	Ecological	Wood preservative	Treated wood
Special study	Honey bee oral toxicity (adults)[13]	TGAI	12	Ecological	Lawn, turf, surface soil, sidewalk, parking lot, patio, ant hill insecticide	Residential lawn and impervious surface

[10] Results from studies conducted using *Chironomus dilutus*, *Hyalella azteca*, and *Leptocheirus plumulosus* are expected to be required to satisfy this anticipated requirement

[11] Results from studies conducted using an upland game species and a waterfowl species are expected to be required to satisfy this anticipated requirement.

[12] Protocol modifying study using wood should be submitted for review prior to conduct of the study.

GLN	Study Name	Test Substance[7]	Time Frame (Measured in months from DCI Receipt)	Risk Assessment(s) Data Will Support	Use Site(s) Triggering Anticipated Data Requirement	Applicable Exposure Scenario
Special study	Honey bee oral toxicity (larvae) [13]	TGAI	12	Ecological	use	
850.4100	Seedling emergence (terrestrial plants)[14]	TGAI	12	Ecological	Lawn, turf, surface soil, sidewalk, parking lot, patio, ant hill insecticide use; Exterior roof, siding, fence, and deck algaecide and antimicrobial treatment	Residential lawn and impervious surface; Exterior building and structure treatment
850.4150	Vegetative vigor (terrestrial plants) [14]	TGAI	12	Ecological		
850.6100	Environmental Chemistry Methods and Associated Independent Laboratory Validation for water	TGAI	12	Ecological	Lawn, turf, surface soil, sidewalk, parking lot, patio, ant hill insecticide use	Residential lawn and impervious surface; Exterior building and structure treatment
875.1700	Product Use Information	TGAI	12	Human Health	All	All
870.2300	Indoor Surface Residues	TGAI	12	Human Health	Residential and Public Access Sites	Incidental oral exposure to disinfected floors.
870.3465	Inhalation Toxicity, 90 day	TGAI	24	Human Health	All	All
Non-Guideline	Paint Chamber Emissions Study	TGAI	12	Human Health	Paints	Inhalation exposure following application of treated paints.
Studies Expected to be Required through the Anticipated Post-RED DCI						
850.1075	Acute toxicity estuarine/marine fish	TGAI	12	Ecological	All	Industrial processes; DtD premise and equipment uses; Material preservatives with DtD releases; Residential lawn and impervious surface; Treated wood; Exterior paint/stain; Exterior building and structure treatment; Residential lawn and impervious surface
850.1300	Aquatic invertebrate life cycle (freshwater)[15]	TGAI	12			
850.1400	Fish early life stage[16,17]	TGAI	12			
870.7800	Immunotoxicity	TGAI	12	Human Health	All	All

[13] Based on the "White Paper in Support of the Proposed Risk Assessment Process for Bees" as submitted to the FIFRA Scientific Advisory Panel, docket number EPA-HQ-OPP-2012-0543-0004 at http://www.regulations.gov.

[14] Plant toxicity data with a monocot species, rice, have been submitted. Additional data are anticipated to be needed for six species of dicots (from at least four families; one species must be soybean) and three species of monocots (from at least two families; one species must be corn). Of the species selected to satisfy this anticipated data need, at least one test species should be a root crop (either a monocot such as onion or a dicot such as carrot, table beet, or sugar beet).

[15] Results from an acceptable *Daphnia* life cycle test may be used to calculate a chronic toxicity endpoint for estuarine/marine invertebrates.

[16] Results from studies conducted using a freshwater species and a saltwater species are expected to be required to satisfy this anticipated requirement.

[17] Results from an acceptable freshwater fish early life stage test may be used to calculate a chronic toxicity endpoint for estuarine/marine fish.

GLN	Study Name	Test Substance[7]	Time Frame (Measured in months from DCI Receipt)	Risk Assessment(s) Data Will Support	Use Site(s) Triggering Anticipated Data Requirement	Applicable Exposure Scenario
875.1200	Indoor Dermal Exposure	TGAI	24	Human Health	Material preservation, industrial process treatment, hard surface disinfection, preserved paints, sapstain treatment, carpets, air sanitizers, fingerpaints	Occupational handler scenarios: (1) Open pour liquids and soluble powders for material preservation and industrial process treatment[18], (2) Low pressure/high pressure handwand, aerosol can, trigger sprayer, mop and wipe for hard surface disinfection, (3) Handheld fogging for hard surface disinfection[19], (4) Brush, roller and spray for preserved paints, (5) Dip and spray for sapstain treatment. Residential handler scenarios: (1) Aerosol can, trigger sprayer, mop and wipe for hard surfaces and carpets, (2) Aerosol can air sanitizers, (3) Brush, roller and spray for preserved paints, (4) Hand application of finger paints.

[18] If labels are amended to require closed loading and delivery systems for liquid products and water soluble packaging for solid products used for material preservation and industrial process treatment, the agency may consider waiving the need for the exposure study for open pouring of liquids and soluble powders.
[19] If labels are amended to require that fogging be done only by automatic equipment, the agency may consider waiving the need for the exposure study for handheld fogging.

GLN	Study Name	Test Substance[7]	Time Frame (Measured in months from DCI Receipt)	Risk Assessment(s) Data Will Support	Use Site(s) Triggering Anticipated Data Requirement	Applicable Exposure Scenario
875.1400	Indoor Inhalation Exposure	TGAI	24	Human Health	Material preservation, industrial process treatment, hard surface disinfection, preserved paints, sapstain treatment, carpets, air sanitizers, fingerpaints	Occupational handler scenarios: (1) Open pour liquids and soluble powders for material preservation and industrial process treatment[18], (2) Low pressure/high pressure handwand, aerosol can, trigger sprayer, mop and wipe for hard surface disinfection, (3) Handheld fogging for hard surface disinfection[19], (4) Brush, roller and spray for preserved paints, (5) Dip and spray for sapstain treatment. Residential handler scenarios: (1) Aerosol can, trigger sprayer, mop and wipe for hard surfaces and carpets, (2) Aerosol can air sanitizers, (3) Brush, roller and spray for preserved paints, (4) Hand application of finger paints.
875.2800	Descriptions of Human Activity	TGAI	12	Human Health	All	All
Special Study	Migration Study for Plastics and Polymers	TGAI	12	Human Health	Material preservation of plastics and polymers	Incidental Oral Exposure to Household Items and Toys Manufactured from Plastics and Polymers preserved with *o*PP.
Studies no longer anticipated as needed						
875.1600	Applicator Exposure Monitoring Data Reporting					

3 Human Health Risk Assessment

EPA anticipates the need to conduct a human health risk assessment for *o*PP and its salts. EPA expects to require additional data for use in conducting the registration review.

3.1 Existing Toxicological Endpoints

EPA anticipates the need to revise the existing toxicological endpoints as part of this registration review. The toxicological points of departure (PODs) for *o*PP are included in Table 9. These PODs were established in 2004 by the Antimicrobials Division's Toxicology Endpoint Selection Committee (ADTC). These PODs have not been updated. All information, including existing toxicology studies, valid scientific literature and the studies that are expected to be required for registration review will be considered in the final risk assessment for *o*PP and its salts.

Table 9 – Existing Toxicological Endpoints for *o*PP

Exposure Scenario	Dose Used in Risk Assessment (mg/kg/day)	Target Margin of Exposure (MOE), Uncertainty Factor (UF), FQPA Safety Factor (SF)	Study and Toxicological Effects
Dietary Risk Assessments			
Acute Dietary (general population and females 13- 49)	No appropriate endpoints were identified that represent a single dose effect. Therefore, this risk assessment is not required.		
Chronic Dietary (all populations)	**NOAEL** = 39 mg/kg/day (43% dermal absorption)	**FQPA SF** = 1 **UF** = 100 (10x inter-species extrapolation, 10x intra-species variation) **Chronic RfD** = 0.39 mg/kg/day **Chronic PAD** = 0.39 mg/kg/day	Combined oral toxicity/carcinogenicity study in rats (MRID 43954301, 44852701, 44832201) LOAEL of 200 mg/kg/day based upon decreased body weight, body weight gain, food consumption and food efficiency, increased clinical and gross pathological signs of toxicity.
Non-Dietary Risk Assessments			
Incidental Oral Short-Term (1 - 30 days)	**NOAEL (maternal)** = 100 mg/kg/day	**Target MOE** = 100 **FQPA SF** = 1 **UF** = 100 (10x inter-species extrapolation, 10x intra-species variation)	Developmental (gavage) toxicity studies in rats (MRID 00067616, 92154037) and rabbits (MRID 41925003; co-critical developmental toxicity study) Maternal LOAEL of 300 mg/kg/day based upon clinical observations of toxicity, decreased weight gain, food consumption and food efficiency observed in the rat developmental toxicity study.
Incidental Oral Intermediate-Term (1 - 6 months)	**NOAEL** = 39 mg/kg/day	**Target MOE** = 100 **FQPA SF** = 1 **UF** = 100 (10x inter-species extrapolation, 10x intra-species variation)	Combined oral toxicity/carcinogenicity study in rats (MRID 43954301, 44852701, 44832201) LOAEL of 200 mg/kg/day based upon decreased body weight, body weight gain, food consumption and food efficiency, increased clinical and gross pathological signs of toxicity.
Dermal Short-Term (1 - 30 days) (residential and occupational)	**NOAEL (dermal)** = 100 mg/kg/day (200 $\mu g/cm^2$) [A]	**Target MOE** = 100 **FQPA SF** = 1 **UF** = 100 (10x inter-species extrapolation, 10x intra-species variation)	21-Day Dermal toxicity study in rats (MRID 42881901) LOAEL (dermal) of 500 mg/kg/day based upon dermal irritation (erythema, scaling) at the site of test substance application.
Dermal	**NOAEL** = 39	**Target MOE** = 100	Combined oral toxicity/carcinogenicity study in

Exposure Scenario	Dose Used in Risk Assessment (mg/kg/day)	Target Margin of Exposure (MOE), Uncertainty Factor (UF), FQPA Safety Factor (SF)	Study and Toxicological Effects
Intermediate- and Long-Term (1 - 6 months and >6 months) (residential and occupational)	mg/kg/day [B]	**FQPA SF** = 1 **UF** = 100 (10x inter-species extrapolation, 10x intra-species variation)	rats (MRID 43954301, 44852701, 44832201) LOAEL of 200 mg/kg/day based upon decreased body weight, body weight gain, food consumption and food efficiency (effects observed as early as 13 weeks in this study), increased clinical and gross pathological signs of toxicity.
Inhalation Short-Term (1 - 30 days) (residential and occupational)	**NOAEL (maternal)** = 100 mg/kg/day [C]	**Target MOE** = 100 **FQPA SF** = 1 **UF** = 100 (10x inter-species extrapolation, 10x intra-species variation) **Note:** an additional 10x is necessary for route extrapolation. If results are below a MOE of 1,000, a confirmatory inhalation study may be required	Developmental (gavage) toxicity studies in rats (MRID 00067616, 92154037) and rabbits (MRID 41925003; co-critical developmental toxicity study) Maternal LOAEL of 300 mg/kg/day based upon clinical observations of toxicity, decreased weight gain, food consumption and food efficiency observed in the rat developmental toxicity study.
Inhalation Intermediate- and Long-Term (1 - 6 months and >6 months) (residential and occupational)	**NOAEL** = 39 mg/kg/day [C]	**Target MOE** = 100 **FQPA SF** = 1 **UF** = 100 (10x inter-species extrapolation, 10x intra-species variation) **Note:** an additional 10x is necessary for route extrapolation. If results are below a MOE of 1,000, a confirmatory inhalation study may be required	Combined oral toxicity/carcinogenicity study in rats (MRID 43954301, 44852701, 44832201) LOAEL of 200 mg/kg/day based upon decreased body weight, body weight gain, food consumption and food efficiency (effects observed as early as 13 weeks in this study), increased clinical and gross pathological signs of toxicity.
Cancer (oral, dermal, inhalation)	**Classification:** Ortho phenylphenol is classified as "Not likely to be carcinogenic below a specific dose range, without quantification of risk." (OPP CARC)		

UF = uncertainty factor, DB UF = data base uncertainty factor, FQPA SF = special FQPA safety factor, NOAEL = no observed adverse effect level, LOAEL = lowest observed adverse effect level, PAD = population adjusted dose (a = acute, c = chronic), RfD = reference dose, MOE = margin of exposure

[A] $\left(100\ \text{mg/kg rat} \times 0.200\ \text{kg rat} \times 1000\ \mu\text{g/mg}\right) \Big/ \left(100\ \text{cm}^2\ \text{area of rat dosed}\right) = 200\ \mu\text{g/cm}^2$

[B] A dermal absorption factor of 43% was chosen based on the results of a submitted study (Timchalk *et al.*, 1996) in humans.

[C] The inhalation absorption factor of 100% (default value, assuming oral and inhalation absorption are equivalent) is used as an assumption since an oral endpoint was selected for the inhalation exposure scenarios.

3.2 **Dietary Exposure**

The Agency anticipates the need to revise the dietary (food) assessment conducted in support of the 2006 RED. Uses of *o*PP and its salts that may result in dietary exposures include sanitization use on counter tops, tables, refrigerators; on livestock premises; as a preservative in papermaking; as a preservative in adhesives; on mushroom premises; and as a postharvest fruit and vegetable coating to control storage pathogens.

Dietary risk is characterized in terms of the Population Adjusted Dose (PAD), which reflects the reference dose (RfD), either acute or chronic, that has been adjusted to account for the FQPA Safety Factor (SF). This calculation is performed for each population subgroup for which an endpoint exists. A risk estimate that is less than 100% of the acute or chronic PAD is not of concern. Acute dietary risk for *o*PP and salts will not be assessed because there are no adverse systemic effects attributable to a single dose. Chronic dietary risk for *o*PP and salts will be assessed by comparing dietary exposure estimates expressed in mg/kg/day to the chronic Population Adjusted Dose (cPAD).

3.2.1 **Tolerance Information**

EPA has established a tolerance exemption at 40 CFR 180.920 for use of Na-*o*PP as an intentionally-added inert ingredient (preservative) in pesticide formulations not to exceed 0.1% of the formulation to be applied to growing crops only. In addition, tolerances have been established (40 CFR 180.129) for the combined residues of *o*PP and Na-*o*PP from postharvest application on apple, cantaloupe, carrot, cherry, citrus fruit, cucumber, lemon, nectarine, orange, bell pepper, peach, pear, pineapple, plum, sweet potato, and tomato.

The Food & Drug Administration (FDA) has established a number of food additive regulations for *o*PP and Na-*o*PP. For *o*PP, regulations have been established as a (an):

- Fungicide at ≤0.01% by weight of the base polymer poly(phenyleneterephthalamide) used as a coating to finish fibers and yarn for single and repeat-use food contact (21 CFR 177.1632);
- Miscellaneous material to formulate defoaming agents used in paper and paperboard production (21 CFR 176.210);
- Antioxidant/antioxonant to manufacture rubber articles for repeat-use food contact (21 CFR 177.2600);
- Preservative in the manufacture of food-contact adhesives (21 CFR 175.105); and
- Food contact sanitizer at ≤400 ppm mixed with two other phenols [21 CFR 178.1010(b)(20).

For Na-*o*PP, regulations have been established as a:

- Preservative of coatings only as a component of paper and paperboard in contact with aqueous and fatty foods (21 CFR 176.170);
- Miscellaneous compound in defoaming agents used in the manufacture of paper and paperboard (21 CFR 176.210);
- Preservative in animal glue in articles for food contact (21 CFR 178.3120); and
- Component of closures at ≤0.05 % by weight used with sealing gaskets for food containers (21 CFR 177.1210).

3.2.2 **Food**

EPA anticipates the need to revise the chronic dietary risk assessment conducted in support of the 2006 RED; as there are no adverse systemic effects due to a single dose, an acute dietary risk assessment was not conducted in the 2006 RED and is not expected to be needed for this registration review. In support of the 2006 RED, exposures to residues expected to transfer to

food from various hard nonporous surfaces such as countertops, sinks and stoves were considered. The 2006 RED concluded that there were no risks of concern for chronic dietary exposures to *o*PP and its salts. For all supported uses, chronic dietary exposure estimates presented in the 2006 RED were below the Agency's level of concern (<100% of the cPAD).

3.2.3 **Drinking Water**

Although dietary exposure to *o*PP via drinking water is expected to be minimal due to *o*PP's degradation in soil and via photolysis and its immobility in soil (see Appendix B), the agency will determine whether there is the potential for *o*PP and salts to contaminate drinking water upon evaluation of the anticipated environmental fate studies during the risk assessment stage of this registration review.

3.3 **Occupational and Residential Exposures**

The Agency anticipates the need to revise the occupational and residential assessments conducted in support of the 2006 RED based on an updated exposure database. Uses of *o*PP and its salts that may result in occupational and residential exposures are included in Table 10, Table 11, and Table 12.

3.3.1 **Occupational Handler Exposure**

Occupational handler dermal and inhalation exposures to *o*PP were assessed in the 2006 RED for open pouring for material preservation, low and high pressure handwand application, aerosol can and trigger spray application and mopping and wiping. As there were no chemical-specific exposure data available, exposures were assessed using unit exposure data from the Pesticide Handlers Exposure Database (PHED) and the Chemical Manufacturer's Association (CMA) study, as well as, product label maximum application rates, and related use information. In most scenarios assessed, the respective dermal and inhalation MOEs were not of concern as they were above the target MOE of 100. Some scenarios resulted in MOEs below 100, specifically:

- Agricultural premises, fogging: intermediate-term PPE Total MOE = 98
- Commercial/Institutional premises, wiping: short-term baseline dermal MOE= 74, intermediate-term baseline dermal MOE = 68, and intermediate-term baseline Total MOE = 64.
- Medical premises, mopping: short-term baseline dermal MOE= 93, intermediate-term baseline dermal MOE = 84, and intermediate-term baseline Total MOE = 78.
- Materials Preservatives, liquid pour preservation of textiles: short-term PPE dermal MOE= 92, intermediate-term PPE dermal MOE = 83, and intermediate-term Total MOE = 78.
- Materials Preservatives, painter (applying paint post-preservation), airless sprayer: baseline dermal short-term MOE = 66.

It is important to note that the open pouring of solids for materials preservation was not assessed in the RED, and this scenario could be of concern depending upon the dustiness of the formulation. It is also likely that handheld fogging would result in excessive exposure; however, this scenario was not assessed for the 2006 RED because exposure data were not available.

With respect to agricultural applications, all occupational inhalation MOEs were above the target MOE of 1000, with the exception of fogger application, where the MOE was 880. For dermal

exposures involving agricultural applications, with the use of chemical-resistant gloves, short-term dermal risks were not of concern for handlers. Short-term inhalation risks were not of concern without respiratory protection. Intermediate-/long-term dermal risks were not of concern when chemical-resistant gloves are used and intermediate-/long-term inhalation risks were not of concern.

EPA anticipates the need to revise the occupational handler assessment conducted in support of the 2006 RED. All of the handler scenarios that were assessed in the 2006 RED will need to be revised during registration review upon receipt of the unit exposure data that are anticipated to be required to supplement or replace the unit exposure data that were used in the 2006 RED. In addition, it will be necessary to assess handler exposures for open pouring of soluble powder formulation for material preservation and handler exposures for hand held fogging applications. The occupational handler scenarios to be assessed are listed in Table 10.

Table 10 – Occupational Handler Exposure Scenarios for *o*PP

Scenario	Exposure Route(s)	Duration
Open pour liquids and soluble powders for material preservation and industrial process treatments	Dermal Inhalation	Short, Intermediate, and Long Term
Low pressure handwand, high pressure handwand, aerosol can, trigger sprayer, mop and wipe application for hard surface disinfection	Dermal Inhalation	Short, Intermediate, and Long Term
Handheld fogger application for hard surface disinfection	Dermal Inhalation	Short and Intermediate Term
Brush, roller and spray application of preserved paints	Dermal Inhalation	Short and Intermediate Term
Dip and Spray application for sapstain treatment	Dermal Inhalation	Short, Intermediate and Long Term

3.3.2 Residential Handler Exposures

EPA anticipates the need to revise the residential handler assessment conducted in support of the 2006 RED. Residential handler dermal and inhalation exposures to *o*PP were assessed in the 2006 RED for spraying, mopping and wiping surfaces and for aerosol spray can application for "air sanitization." In all cases, the respective dermal and inhalation MOEs were not of concern.

Residential exposure may occur during application of *o*PP products used as a hard surface disinfectant (e.g., walls, floors, tables, fixtures), to textiles (e.g., clothing, diapers, mattresses, bedding) and to carpets. In addition *o*PP is used as a preservative in finger paints. As such, the Agency has selected representative scenarios for each use site that are believed to be representative of the *o*PP uses, based on end-use product application methods and use amounts. The residential handler exposure scenarios that will be assessed during registration review are listed in Table 11.

Table 11 – Residential Handler Exposure Scenarios for *o*PP

Scenario	Exposure Route(s)	Duration
Aerosol can, trigger sprayer, mop and wipe application to hard surfaces and carpets.	Dermal Inhalation	Short and Intermediate Term
Aerosol can application for air sanitization	Inhalation	Short and Intermediate Term
Brush and roller application of paints treated with *o*PP	Dermal Inhalation	Short Term

Scenario	Exposure Route(s)	Duration
Hand application of fingerpaints treated with *o*PP	Dermal Incidental Oral Inhalation	Short and Intermediate Term

3.3.3 Residential Post-Application Exposures

EPA anticipates the need to revise the residential post-application assessment conducted in support of the 2006 RED. Residential post-application exposures to residues arising from the hard surface disinfection of floors, treated diapers, treated clothing, treated plastic toys and household items, and sanitized air were assessed. The MOEs were not of concern for hard surface disinfection of floors but they were calculated using an assumption of cleaning solution coverage (1000 square feet per gallon) that possibly underestimates exposure and will have to be reassessed using updated values from the AEJV use surveys and/or the AEATF exposure studies. The MOEs were of concern for the clothing and diaper use. The dermal MOEs for the treated clothing ranged from <1 when 100 percent residue transfer was assumed to 17 when 5 percent transfer was assumed. Based on these concerns, the 2006 RED specified that the diaper use was ineligible for reregistration and that label statements be added requiring other treated textile articles be washed after treatment. The MOEs were not of concern for treated toys or household items. The inhalation MOEs for exposure to treated paint and air sanitization were above 100 which means that they were not of concern; however, they were below 1000, which means that the requirement for an inhalation toxicity study was triggered. The residential post application exposure scenarios that will be assessed during registration review are listed in Table 12.

Table 12 – Residential Post-Application Exposure Scenarios for *o*PP

Source of Exposure	Exposure Route(s)	Duration
Floors disinfected with *o*PP	Dermal Incidental Oral	Short and Intermediate Term
Areas painted with paints containing *o*PP	Inhalation (Vapor)	Short and Intermediate Term
Mouthing Toys or Household Items Manufactured from Plastic or Polymers Preserved with *o*PP.	Incidental Oral	Short and Intermediate Term
Air sanitized with *o*PP	Inhalation	Short and Intermediate Term

3.4 Aggregate and Cumulative Exposure

3.4.1 Aggregate Exposures

The Agency anticipates the need to revise the chronic dietary aggregate risk that was conducted in support of the 2006 RED. The calculated total dietary exposure in the 2006 RED showed that there was no risk of concern from dietary sources of exposure. In addition, many of the tolerances and uses listed in the 2006 RED for direct food use of *o*PP have been revoked, which will result in a decrease in total dietary exposures. There is also no significant contribution to dietary risk from drinking water exposure, as was noted in the 2006 RED.

The Agency anticipates the need to revise the short- and intermediate-term aggregate risk assessments for *o*PP. Dermal post-application risks to adults and children showed risks of concern in the 2006 RED and were not included in the dermal aggregate risk calculation. The

mitigation measures discussed in the 2006 RED to reduce dermal risk will need to be evaluated in the registration review risk assessment to determine if dermal post-application risks are mitigated.

3.4.2 Cumulative Exposures

With respect to cumulative exposure, unlike other pesticides for which EPA has followed a cumulative risk approach based on a common mechanism of toxicity, EPA has not made a common mechanism of toxicity finding as to *o*PP and any other substances, and *o*PP does not appear to produce a toxic metabolite common to other substances. For the purposes of this registration review, therefore, EPA has not assumed that *o*PP has a common mechanism of toxicity with other substances. For information regarding EPA's efforts to determine which chemicals have a common mechanism of toxicity and to evaluate the cumulative effects of such chemicals, see the policy statements released by EPA's Office of Pesticide Programs at http://www.epa.gov/pesticides/cumulative/.

4 Environmental Risk Assessment

4.1 Environmental Fate

Ortho-phenyl phenol is a weak acid with a pKa of about 9.5 (MRID 42500204), indicating that *o*PP will primarily exist as the protonated acid in aqueous solution at environmental pH values (5 - 9). The sodium (Na) and potassium (K) salts of *o*PP rapidly dissociate in water releasing sodium and potassium cations (Na^+ and K^+, respectively) and the *ortho*-phenyl phenate anion (oPP^-). The oPP^- anion will readily become protonated forming the neutral or unionized *o*PP. The equilibrium in solution between oPP^- and protonated or unionized *o*PP depends on the pH of the solution. In aqueous medium the following equilibria is expected: at acidic pHs 4 - 6, the parent will essentially be in the protonated or undissociated *o*PP state; at pHs 7 - 9.5, the equilibria will have undissociated *o*PP and some dissociated *o*PP, with increasingly more dissociated *o*PP as pH becomes more alkaline; at pH 9.5, approximately 50% of the *o*PP will be dissociated and 50% undissociated; and at pH >9.5, the tendency is to be in the fully ionized state. Therefore, the fate and transport data supporting *o*PP can be used to support the salts, and similarly the fate and transport data supporting its Na and K salts may be used to support *o*PP. A summary of the fate, transport and degradation of *o*PP and its salts is provided here but details of the studies and information are provided in Appendix B.

4.1.1 *o*PP and its Salts

Ortho-phenyl phenol is hydrolytically stable under abiotic aqueous conditions (MRID 43994201). It does photodegrade in abiotic aqueous medium forming three degradates; the two major degradates, phenylhydroquinone (PHQ) and phenylbenzquinone (PBQ), and hydroxyfuran as a minor degradate were identified (Tajeddine *et al*. 2010). The vapor pressure of *o*PP is 2.00×10^{-3} mm Hg at 25 °C (MRID 41609505 for Na-*o*PP and MRID 41642402 for *o*PP) indicating the potential for volatilization, but the half life of *o*PP in air is estimated to be 0.03 hours using EPISuite version 4.10. The salts are not expected to volatilize based on estimated vapor pressures on the order of 10^{-11} mm Hg (EPISuite version 4.10). *o*PP is immobile on soil surfaces and will not likely contaminate the ground water. Temperature appears to be an important factor in its biodegradation with half-lives ranging from 16 hours to 7 days during the summer season and a little to no biodegradation observed under cooler fall and winter conditions. While there is

information from a specific location indicating potential for aqueous aerobic biodegradation, the information needed to conduct a risk assessment is incomplete since the major biodegradates are not identified. There are no aqueous anaerobic sediment data. These data for *o*PP are anticipated as being required to conduct the risk assessment of *o*PP and its salts. Additionally, to model removal during wastewater treatment, data on the percent removal during wastewater treatment due to sorption and biodegradation (i.e., OCSPP 835.1110, 835.3110, 835.3220, 835.3240, 835.3280) are anticipated to be required.

*o*PP has a log K_{ow} of 3.3, indicating it is potentially bioaccumulative; however, there are no data on bioaccumulation or bioconcentration in aquatic organisms. A bioconcentration study using *o*PP with fish, tracking the major degradates, is anticipated as being required to conduct the risk assessment of *o*PP and its salts.

Na-*o*PP is applied to and leaches easily from sapstain treatment on wood surfaces, and almost 75% is eliminated from wood surfaces within 14 days. The leach rate for 1% treated wood was 71 µg of Na-*o*PP/cm^2 /day, and for 4% treated wood, the leach rate was 192 µg of Na-*o*PP /cm^2 /day; after day 14, the leach rate was 0.5 to 0.2 µg /cm^2/day for both treated woods. A steady state is achieved after 14 days. Since Na-*o*PP ionizes in moist soils, it is more likely to be mobile from such soil surfaces.

Based on the available fate, transformation, and transport data and registered use patterns, aquatic organisms are expected to be exposed to *o*PP and/or its major degradates both in the water column and sediment. There is potential for birds and mammals that eat fish and invertebrates to be exposed via the aquatic food web to *o*PP and its major toxic degradates. Additionally, there are registered uses that will result in exposure of terrestrial wildlife and plants to residues of *o*PP and its salts and major toxic degradates on dietary items through direct application, spray drift, and run-off.

4.1.2 **Photodegradates of *o*PP**

The Agency has used EPI Suite, version 4.1 to estimate physical/chemical as well as some environmental fate characteristics for the major photodegradates PHQ and PBQ.

4.1.2.1 **Phenylhydroxybenzquione (PHQ)**

The estimated physical/chemical property and environmental fate data on this compound from EPI Suite, version 4.1 (See Appendix B) indicates that PHQ is highly water soluble, and its vapor pressure is not of concern for the exposure assessment. Its estimated half life is 15 days in water bodies, and about thirty days in soils, making it not that persistent in these environmental media. It could be stable and persistent in sediments with an estimated half life of 135 days. It is not stable in air, and the estimated half life is less than six hours in air. It is not likely to be bioaccumulative as its log K_{ow} is less than 3. It appears to not readily biodegrade and may not be removed from wastewater treatment. It has a high K_{oc} value making it immobile in soils; thus the probability of this chemical migrating to ground water is low, and so ground water contamination is not likely to happen. However, aquatic benthic organisms may be exposed.

4.1.2.2 **Phenylbenzquinone (PBQ)**

The estimated data on PBQ (EPI Suite, version 4.1) indicate that this substance is highly water soluble, and its vapor pressure is not of concern for the exposure assessment. Its estimated half life is 15 days in water bodies and about thirty days in soils, making it not that persistent in these

environmental media. It could be stable and persistent in sediments with an estimated half life of 135 days. It is not stable in air, and the estimated half life is less than eight hours in air. It is not likely to be bioaccumulative as its log K_{ow} is less than 2. It appears to be not readily biodegradable and may not be removed from the wastewater treatment plants. It has a high K_{oc} value making it immobile in soils; thus the probability of this chemical migrating to ground water is low, and so ground water contamination is not likely to happen.

At this time the Agency cannot determine environmental risk concerns for these photodegradates, and no fate assessment was conducted. The Agency anticipates using a total toxic residue approach. If any fate data on these degradates becomes available which indicate environmental risk concerns, the Agency anticipates requiring additional fate data.

4.1.3 Water Quality

Ortho-phenyl phenol and its salts, Na-*o*PP and K-*o*PP, are not identified as a cause of impairment for any water bodies listed as impaired under section 303(d) of the Clean Water Act[20]. In addition, no Total Maximum Daily Loads (TMDL) have been developed for *o*PP, Na-*o*PP, and K-*o*PP [21]. More information on impaired water bodies and TMDLs can be found at EPA's website[22].

4.2 Conceptual Models for Environmental Exposure Pathways

4.2.1 Residential Insecticidal Use Patterns

The environmental fate properties and use patterns of *o*PP and its salts indicate that direct spray, spray drift, atmospheric deposition, and run-off represent potential transport mechanisms of *o*PP and its salts to aquatic and terrestrial organisms.

For terrestrial vertebrates, the major route of exposure to *o*PP and its salts is considered to be via dietary ingestion of food items such as seeds, plants, and/or animals that have *o*PP (and its salts) residues as a result of direct application, spray drift, and run-off. Exposure of birds and mammals to *o*PP and its salts through the consumption of drinking water alone is also considered to be an exposure pathway of concern based on the results of EFED's Screening Imbibition Program (SIP v. 1.0). There is uncertainty regarding whether exposure to terrestrial vertebrates via inhalation is an exposure pathway of concern given the lack of acute inhalation toxicity data needed for analysis using EFED's Screening Tool for Inhalation Risk (STIR v. 1.0). SIP and STIR are described in detail at: http://www.epa.gov/oppefed1/models/terrestrial/index.htm.

For terrestrial invertebrates, the major routes of exposure to *o*PP and its salts are considered to be direct contact as a result of direct application and spray drift and dietary ingestion of plants, animals, and/or soil that have *o*PP (and its salts) residues as a result of direct application, spray drift, and run-off.

For aquatic animal species, the major route of exposure to *o*PP and its salts is considered to be uptake via the respiratory surface (gills) or the integument from surface water/sediment that has *o*PP (and its salts) residues as a result of spray drift and run-off.

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[20] http://iaspub.epa.gov/tmdl_waters10/attains_nation_cy.cause_detail_303d?p_cause_group_id=885

[21] http://iaspub.epa.gov/tmdl_waters10/attains_nation.tmdl_pollutant_detail?p_pollutant_group_id=885&p_pollutant_group_name=PESTICIDES

[22] http://www.epa.gov/owow/tmdl/

For terrestrial (upland and semi-aquatic) non-target plants, the major routes of exposure to *o*PP and its salts are considered to be direct contact as a result of direct application and spray drift and root uptake via soil contaminated via spray drift and run-off.

For aquatic plants, the major route of exposure to *o*PP and its salts is considered to be uptake from surface water/sediment containing *o*PP (and its salts) residues as a result of spray drift and run-off.

4.2.2 **Antimicrobial Use Patterns**

Based on the summary of registered uses of *o*PP and salts presented in Table 8 and physical/chemical property and environmental fate data presented in Appendix B, the Agency has developed conceptual model diagrams for exposure of ecological organisms to *o*PP. These conceptual model diagrams for *o*PP specify the potential routes of exposure, possible ecological receptors, and attribute changes that might occur.

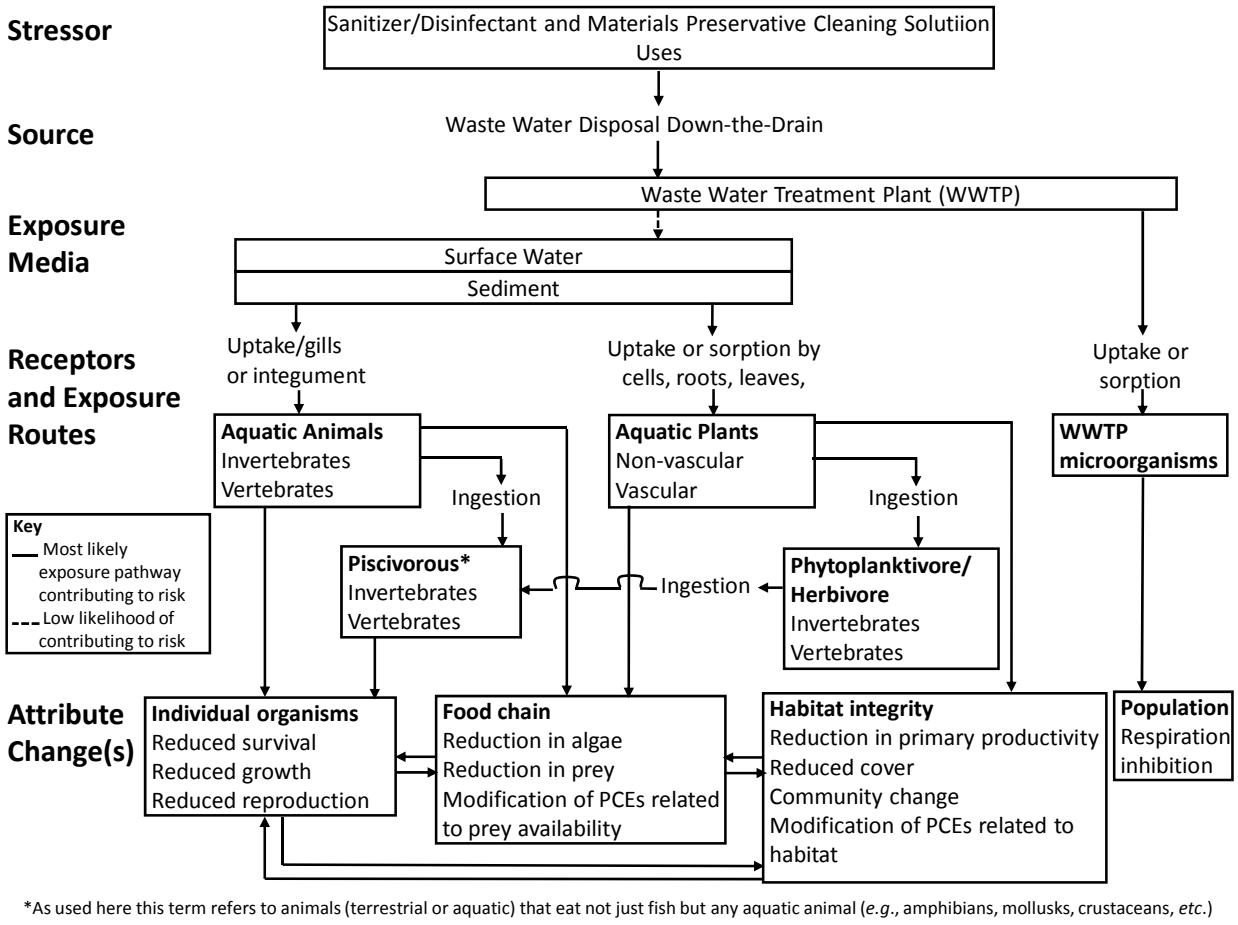
There is some evidence that *o*PP is susceptible to biodegradation during wastewater treatment and in the aquatic environment. Based on studies using activated sludge, *o*PP was determined to be reduced by 50% in acclimated sludge within 3 hours and in unacclimated sludge within 24 hours (MRID 439942-01). In addition, there are studies measuring evolved CO_2 that demonstrate a 50% reduction of *o*PP in river water within a week (MRID 439942-01; Gonsior,1984). This paper did not identify and biodegradates. Based on its log Kow of 3.3, *o*PP may have potential to bioconcentrate in aquatic organisms. One study has indicated that *o*PP can photodegrade to form PBQ and PHQ (MRID 439942-01).

The Agency has previously determined that the use of *o*PP and salts for sapstain treatment of freshly cut lumber has a potential to expose and cause detrimental acute impacts to aquatic organisms, including listed species. Measures to reduce leaching from freshly cut wood and reduce run-off from treatment sites have not yet been sufficiently implemented to reduce the exposure pathways and minimize exposure to aquatic organisms. Impacts from in-service use of treated wood also need to be considered. Chronic exposure of aquatic organisms also is possible and will be assessed when the required data are available. As a wood preservative for treatment to freshly cut lumber, *o*PP also has a potential to adversely affect honey bees that contact the treated wood, but toxicity data are not currently available to assess that potential hazard. Based on its log Kow (3.3), *o*PP has a potential to bioconcentrate in aquatic organisms. *o*PP entering the aquatic environment is expected to adsorb to sediment and may pose a potential risk to benthic organisms.

*o*PP and salts have numerous registered uses. Use sites and corresponding figures of conceptual model diagrams are presented as follows:

- Sanitizer/Disinfectant and Material Preservatives in Cleaning Solutions (Figure 1);
- Antimicrobial Fruit and Vegetable Washes and Food Contact Sanitizer (Figure 2);
- Wood Preservative for Sapstain Control (Figure 3);
- Materials Preservatives in Metal Working Fluids (Figure 4);
- Swimming Pools, Spas, Ornamental Ponds, Aquaria, Waterbed Water (Figures 5a/b);
- Lakes, Ponds, and Reservoirs (Figure 6); and
- Commercial/Industrial Water Cooling Systems; Evaporative Condenser Water Systems; Heat Exchanger Water Systems; Sewage Systems; Industrial Scrubbing Systems; Paper Mill Water Systems; and Air Washer Water Systems (Figure 7);

- Biocides in Oil Drilling Muds and Secondary Recovery Water (Figures 8a/b); and
- Materials Preservatives Other than Those Used in Metal Working Fluids and Cleaning Solutions (Figure 9)



*As used here this term refers to animals (terrestrial or aquatic) that eat not just fish but any aquatic animal (*e.g.*, amphibians, mollusks, crustaceans, *etc.*)

Figure 1 - Conceptual Model for Ecological Exposure and Effects of *o*PP and Salts to Aquatic and Terrestrial Organisms from Sanitizer/Disinfectant and Material Preservative Cleaning Solution Uses

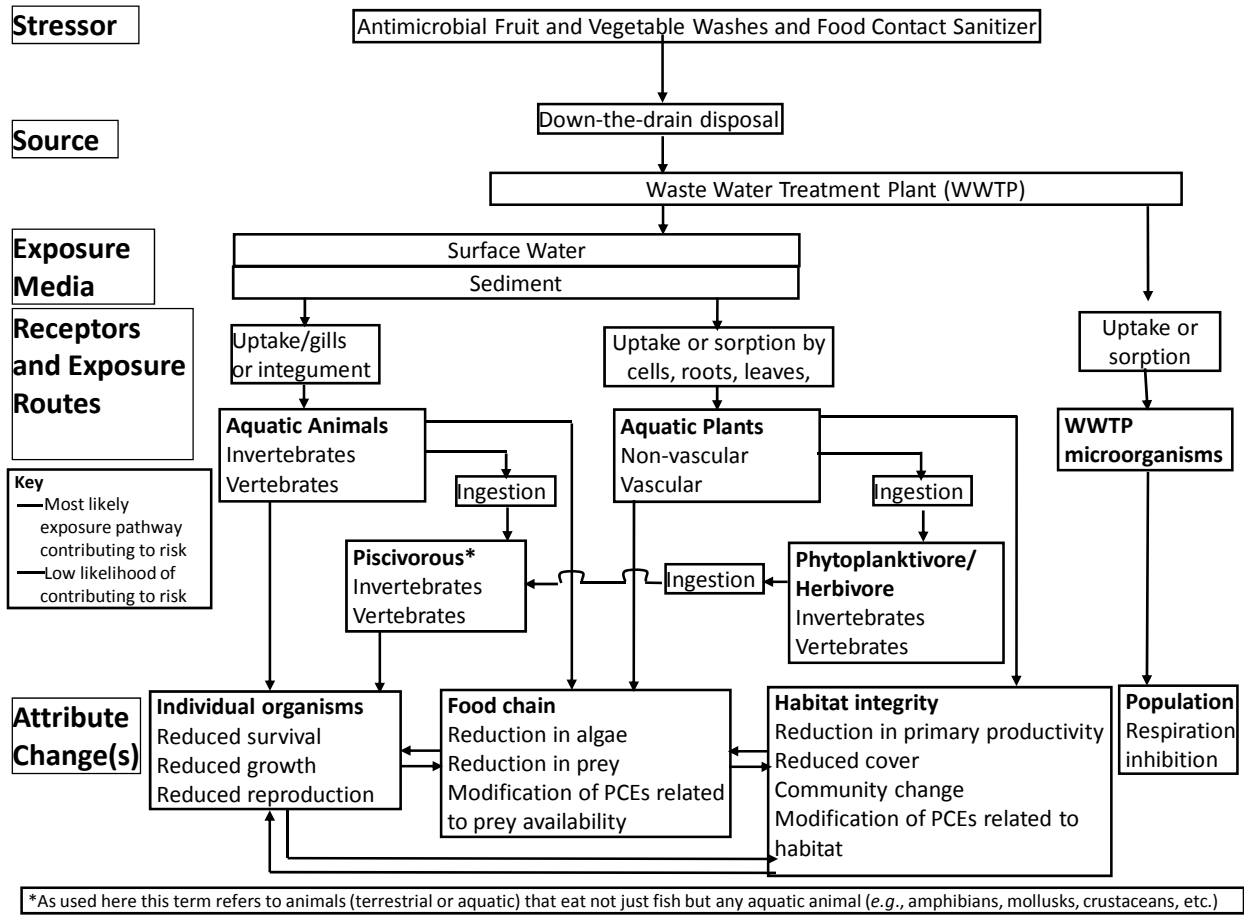
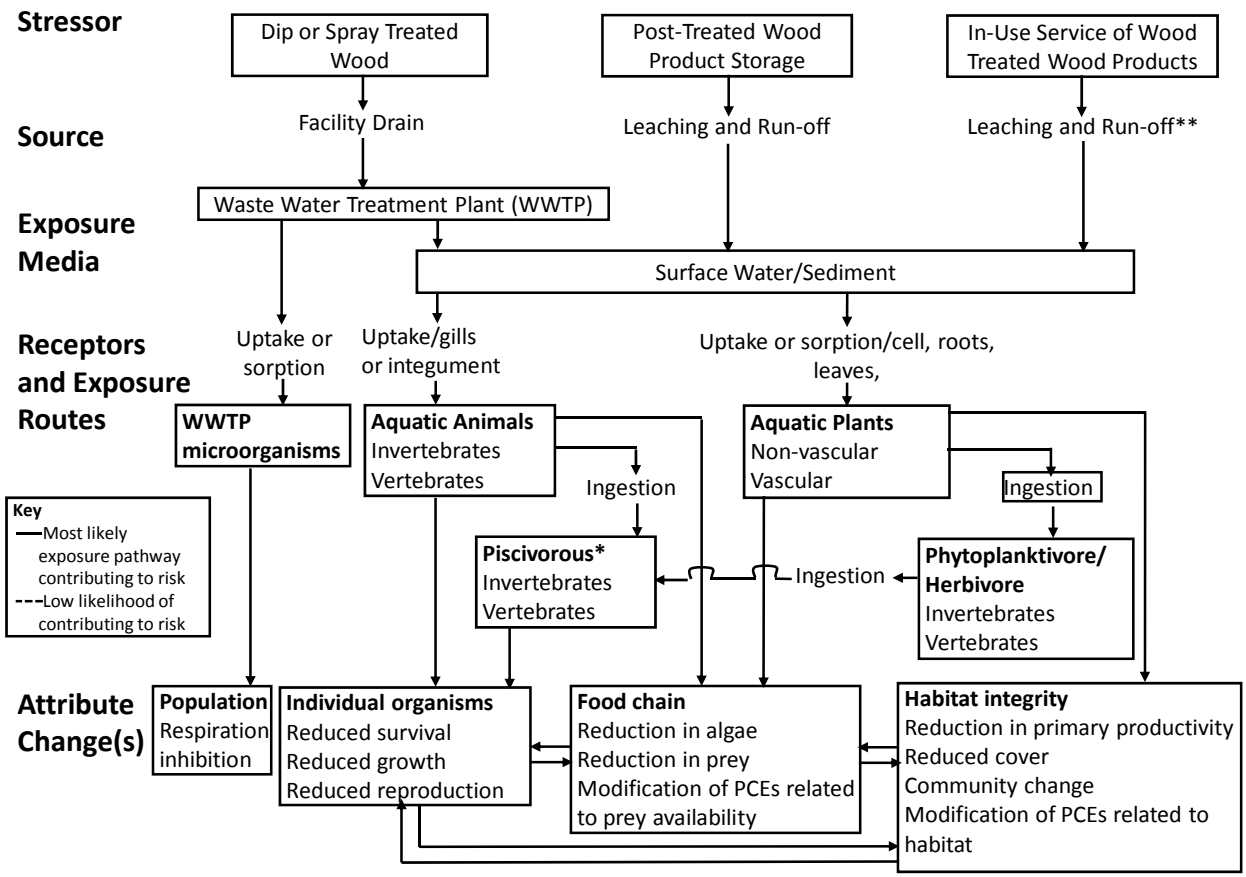


Figure 2 - Conceptual Model for Ecological Exposure and Effects of *o*PP and Salts to Aquatic and Terrestrial Organisms from Antimicrobial Fruit and Vegetable Washes



*As used here this term refers to animals (terrestrial or aquatic) that eat not just fish but any aquatic animal (*e.g.*, amphibians, mollusks, crustaceans, etc.)
**Noise barrier scenario may have releases to WWTP

Figure 3 - Conceptual Model for Ecological Exposure and Effects of *o*PP and Salts to Aquatic and Terrestrial Organisms from Wood Preservatives for Sapstain Control

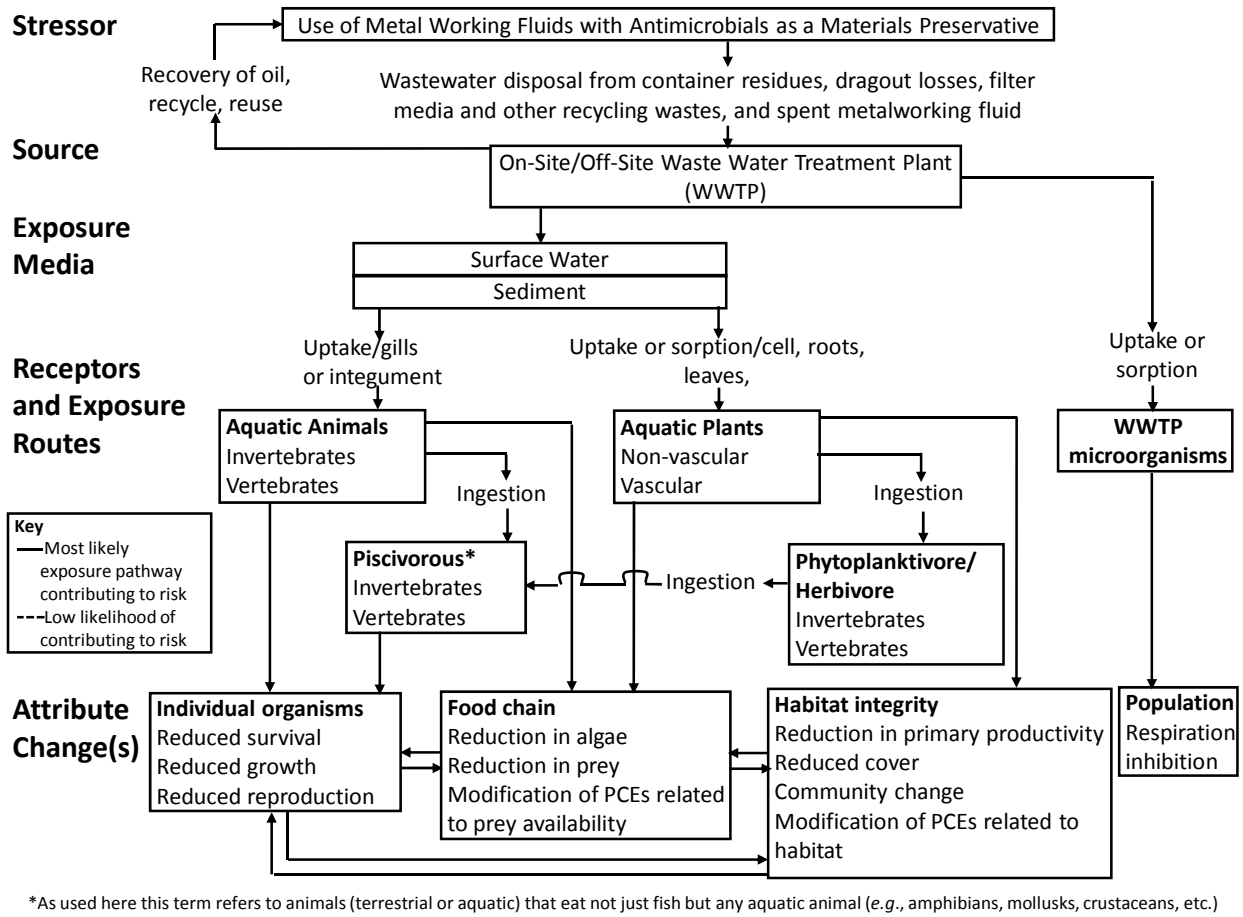


Figure 4 -- Conceptual Model for Ecological Exposure and Effects of *o*PP and Salts to Aquatic and Terrestrial Organisms from Materials Preservatives in Metal Working Fluids

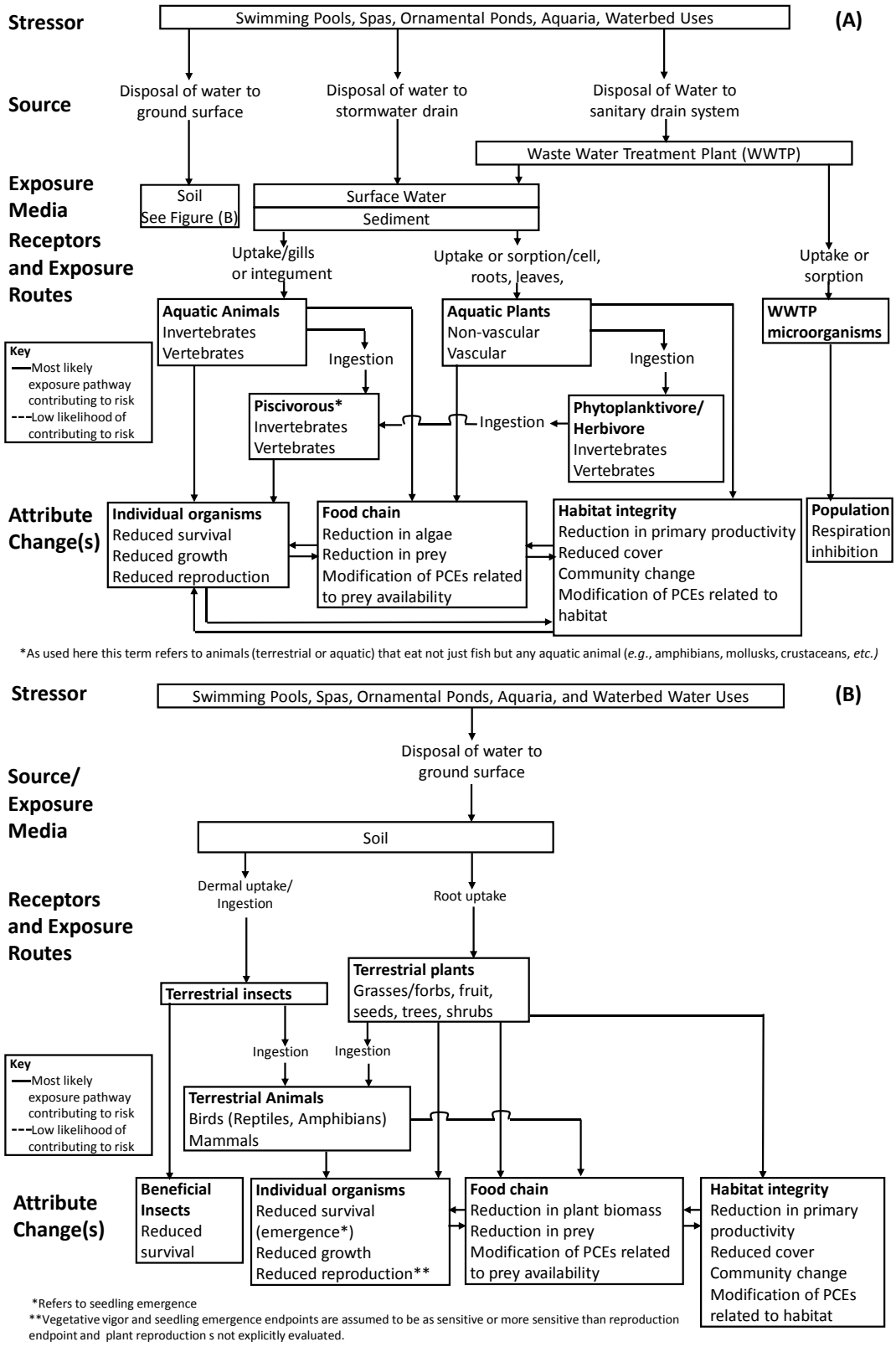


Figure 5 - Conceptual Model for Ecological Exposure and Effects of *o*PP and Salts to Aquatic and Terrestrial Organisms from Swimming Pools, Spas, Ornamental Ponds, Aquaria, and Waterbed Water Uses

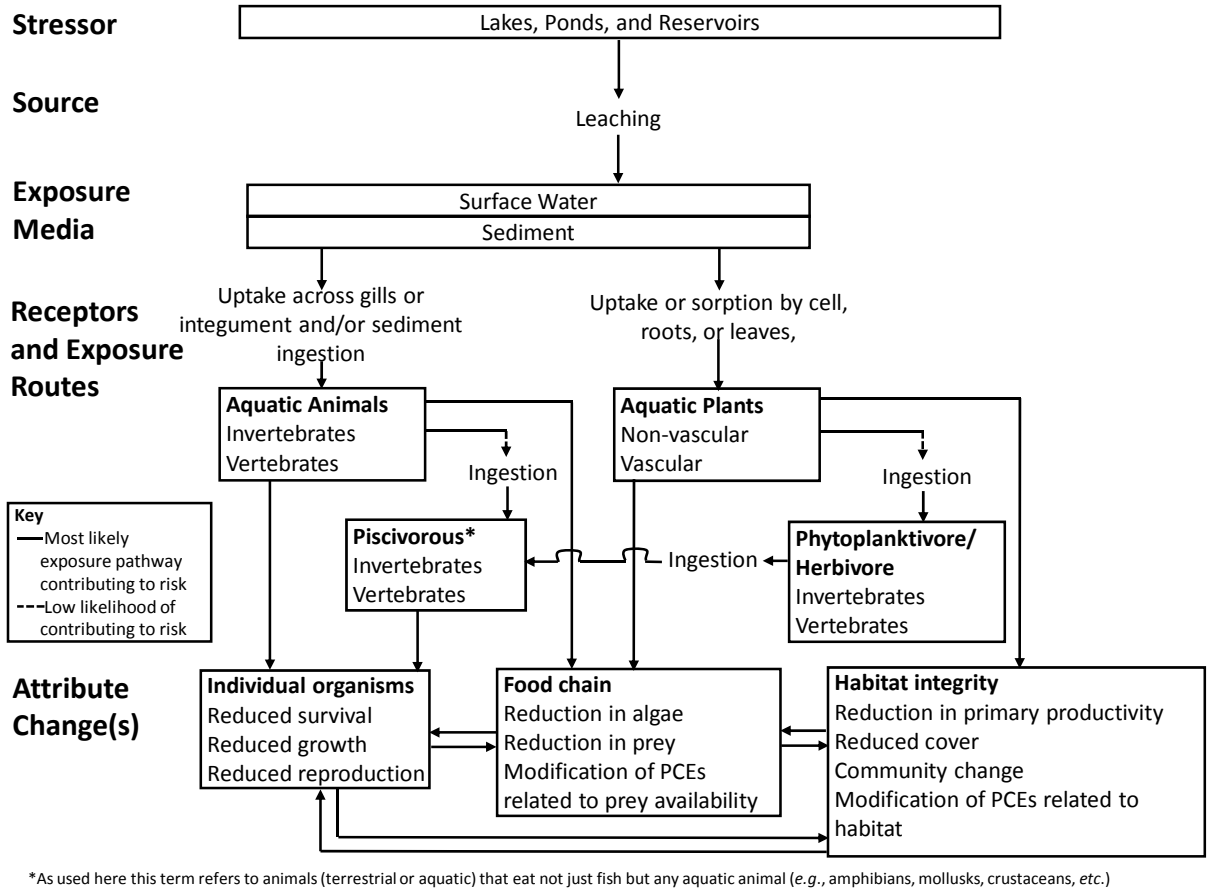
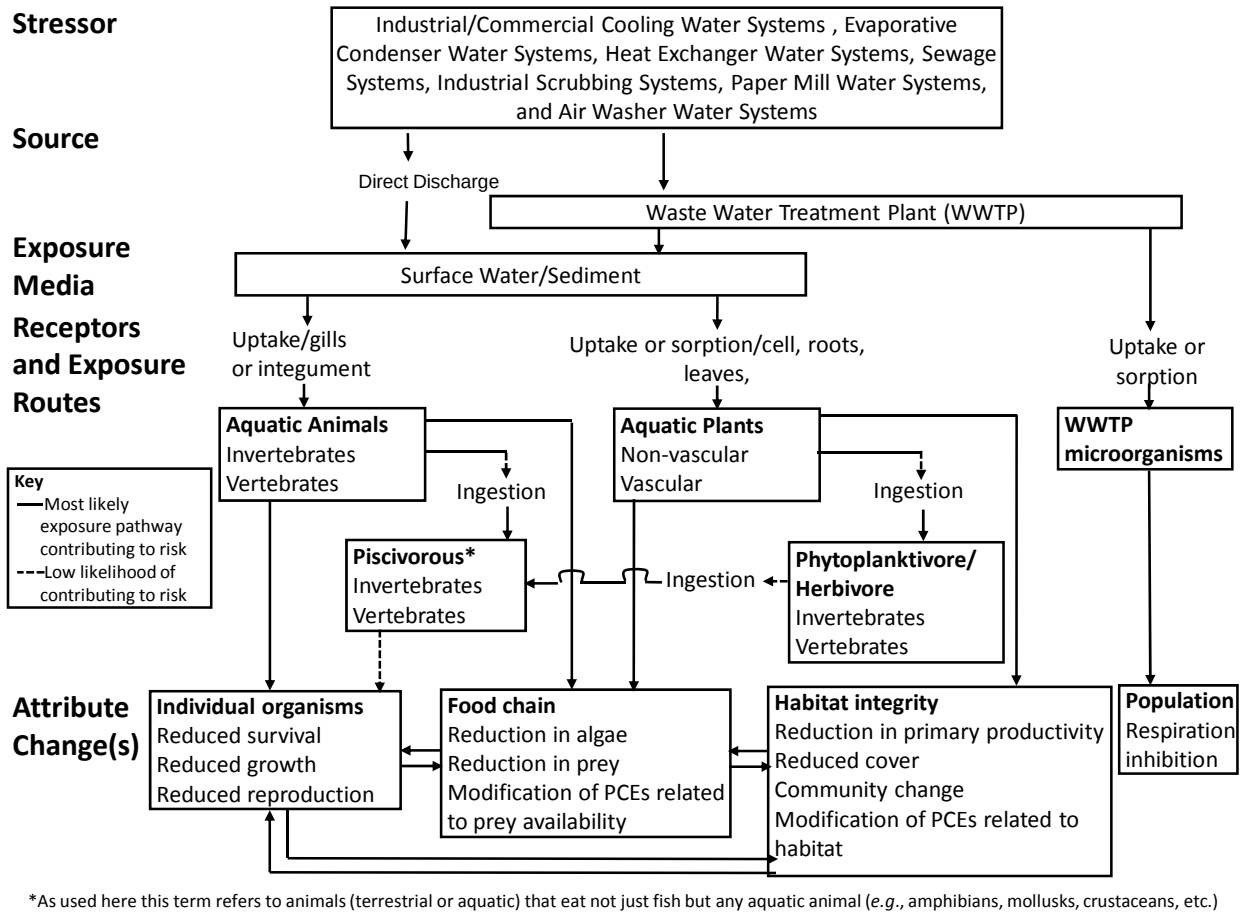
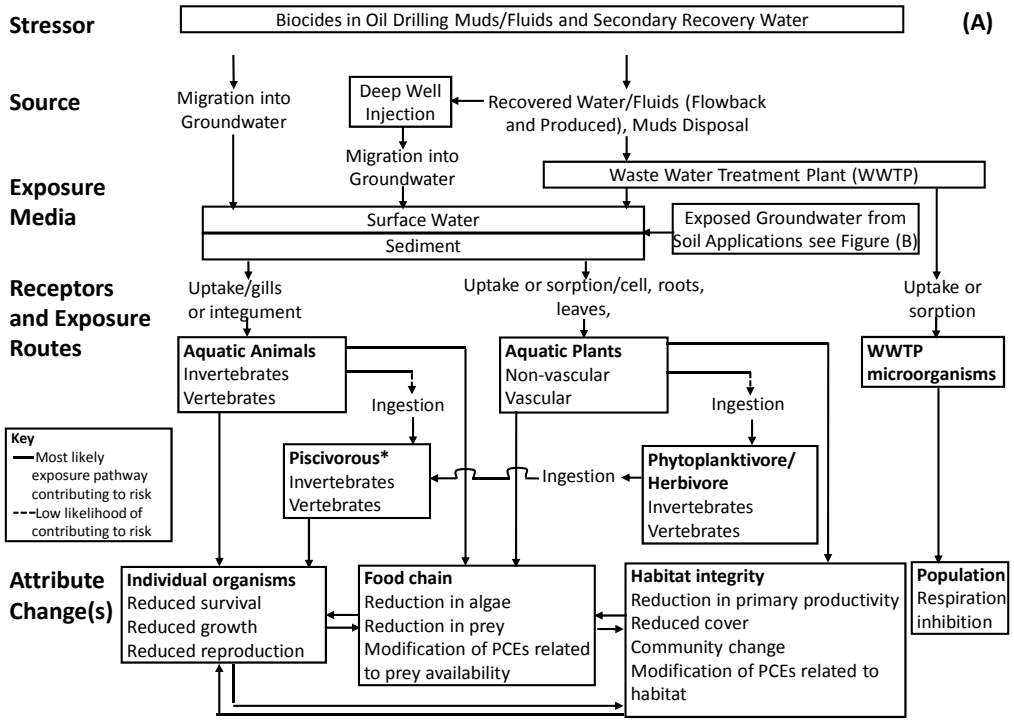


Figure 6 - Conceptual Model for Ecological Exposure and Effects of *o*PP and Salts to Aquatic and Terrestrial Organisms from Lakes, Ponds, and Reservoirs



*As used here this term refers to animals (terrestrial or aquatic) that eat not just fish but any aquatic animal (*e.g.*, amphibians, mollusks, crustaceans, etc.)

Figure 7 - Conceptual Model for Ecological Exposure and Effects of *o*PP and Salts to Aquatic and Terrestrial Organisms from Cooling, Evaporative Condenser, Heat Exchanger, Industrial Scrubbing, and Paper Mill Water Systems



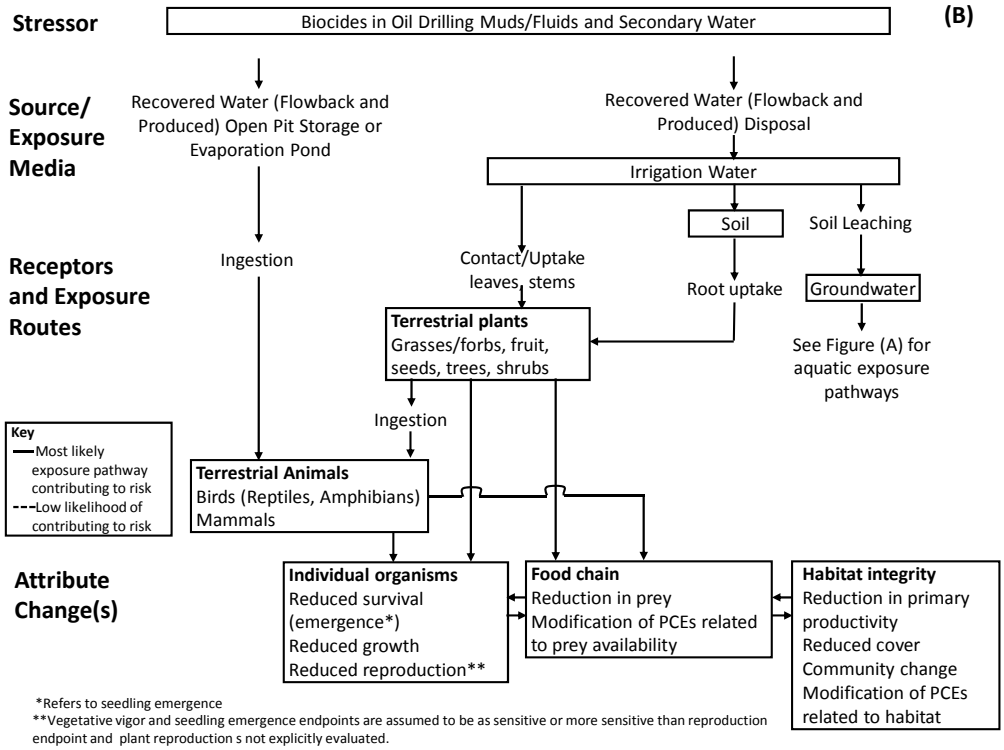


Figure 8 - Conceptual Model for Ecological Exposure and Effects of *o*PP and Salts to Aquatic and Terrestrial Organisms from Biocides in Oil Drilling Muds/Fluids and Secondary Recovery Water

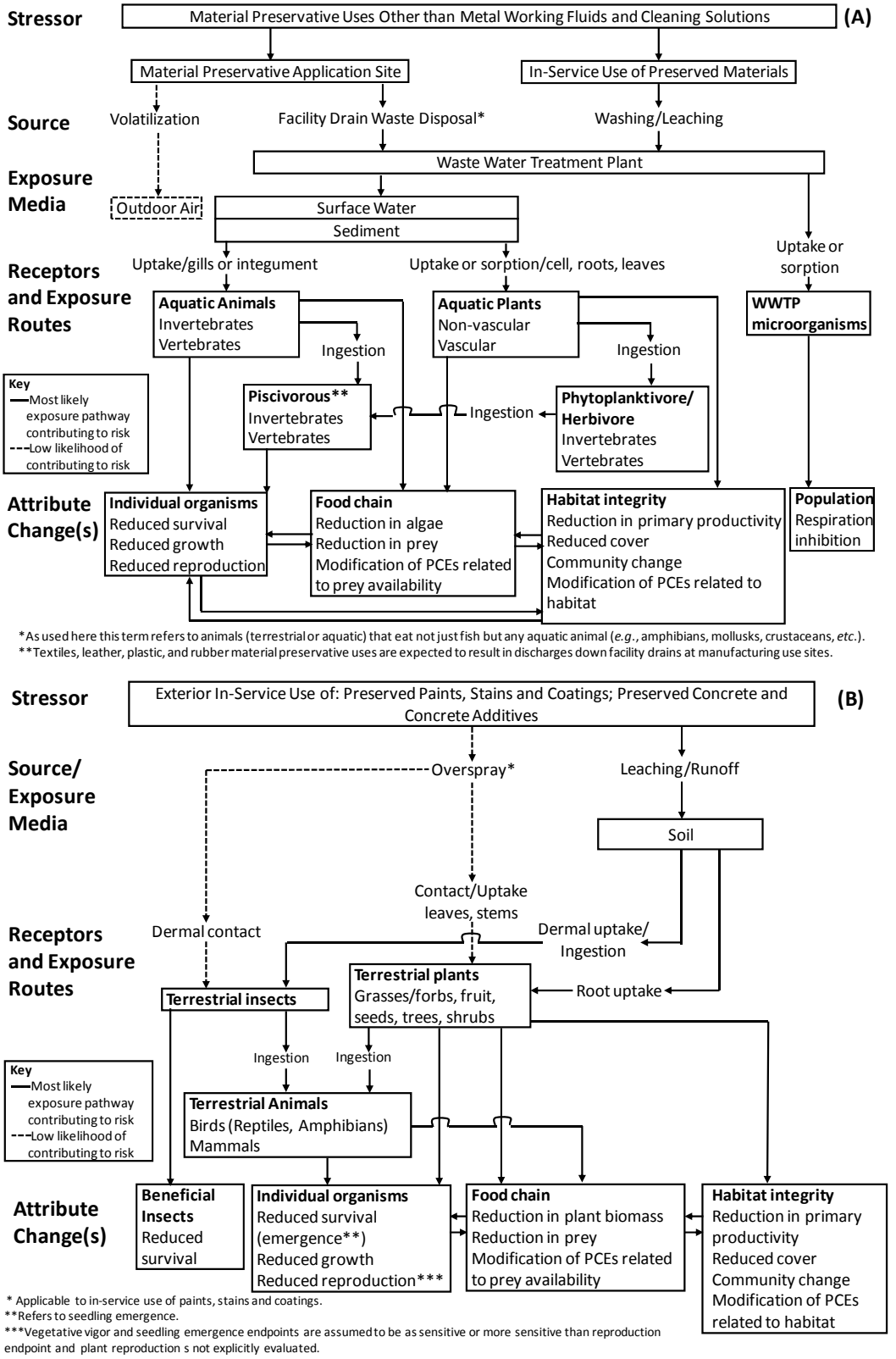


Figure 9 - Conceptual Model for Ecological Exposure and Effects of *o*PP and Salts to Aquatic and Terrestrial Organisms from Material Preservative Uses Other Than Metal Working Fluids and Cleaning Solutions

4.3 Ecological Effects Assessment

In the 2006 RED issued in August of 2006, the Agency conducted an aquatic ecological risk assessment for the antisapstain treatment of Na-*o*PP to freshly cut wood. Based on the toxicity data available at that time, the assessment was limited to acute risks to freshwater organisms, including fish, invertebrates, and algae. Exposure estimates were based on the Agency's use of a sapstain model, which predicts post-treatment pesticide-leachate concentrations in diluted storm-water run-off that may enter the aquatic environment. The LOC for acute risk was exceeded for freshwater fish, freshwater invertebrates, and aquatic plants. Acute risk to estuarine/marine organisms and chronic risks to all aquatic organisms was not assessed due to lack of toxicity data. Possible acute and chronic risks from the in-service use of treated wood were not assessed. No other uses have been assessed.

To mitigate the risks identified in the RED, the Agency specified that product labels with an antisapstain use bear the following label statement: "*Treated lumber must be stored under cover, indoors, or at least 100 feet from any pond, lake, stream, wetland, or river to prevent possible run-off of the product into the waterway. Treated lumber stored within 100 feet of a pond, lake, steam, or river must be either covered with plastic or surrounded by a berm to prevent surface water run-off into the nearby waterway. If a berm or curb is used around the site, it should consist of impermeable material (clay, asphalt, concrete) and be of sufficient height to prevent run-off during heavy rainfall events.*"

The Agency has not conducted a risk assessment that supports a complete endangered species determination for *o*PP and salts. The ecological risk assessment planned during registration review will allow the Agency to refine its risk assessment to determine whether uses of *o*PP and salts have 'no effect' or 'may affect' federally listed threatened or endangered species (listed species) or their designated critical habitats. When an assessment concludes that a pesticide's use 'may affect' a listed species or its designated critical habitat, the Agency will consult with the U.S. Fish and Wildlife Service and/or National Marine Fisheries Services (the Services), as appropriate.

4.3.1 Mechanism of Action

The Agency found no information on the mechanisms of action of *o*PP in terrestrial and aquatic plants and animals.

4.3.2 Measures of Effect (Ecotoxicology Endpoints)

Ecological effects data are used as measures of direct and indirect effects to aquatic and terrestrial organisms. Acute and chronic toxicity data will be used to evaluate the potential direct and indirect effects of *o*PP and salts to plants and animals. Relevant data from the open literature available in ECOTOX also may be used to evaluate potential direct and indirect effects.

All data requirements and available ecotoxicity endpoints from studies submitted by registrants are tabulated in Appendix C. The Agency uses the most sensitive of these endpoints for assessing risk to each terrestrial and aquatic receptor group. The endpoints selected for the risk assessment for *o*PP and salts are provided in Table 13. Data gaps also are indicated.

Table 13 – Selected Ecological Effects Endpoints for the Ecological Risk Assessment

Receptor Group	Surrogate Species	Risk Scenario	Toxicity Endpoint	MRID Reference

Receptor Group	Surrogate Species	Risk Scenario	Toxicity Endpoint	MRID Reference
Freshwater fish	Bluegill	Acute	96-h LC_{50} = 2.74 mg aeL	110232
		Chronic	Data gap	--
Freshwater invertebrates	Waterflea	Acute	48-h EC_{50} = 2.4 mg ae/L	110222
		Chronic	Data gap	--
Estuarine/marine fish	--	Acute	Data gap	--
		Chronic		--
Estuarine/marine invertebrates	Mysid shrimp	Acute	96-h LC_{50} = 0.28 mg ae/L	467512-03
		Chronic	Data gap	--
	Mollusk	Acute	48-h IC_{50} = 0.66 mg ae/L	25816
Sediment-dwelling invertebrates	Freshwater	Chronic	Data gap	--
Aquatic macrophytes/ Aquatic non-vascular plants	Green algae	Non-listed	EC_{50} = 1.39 mg ae/L	456882-01
	Blue-green algae	Listed	NOAEC = 0.03 mg ae/L	
Non-emergent aquatic macrophytes/Aquatic vascular plants	*Lemna*	Non-listed	7-day IC_{50} = 5.5 ppm ae/L	467512-09
		Listed	7-day IC_{05} = 0.73 ppm ae/L	
Emergent rooted aquatic macrophytes-Seedling emergence	Rice	Non-listed	EC_{25} > 886 ppm ae	467512-07
		Listed	NOAEC = 886 ppm ae (7% emergence inhibition)	
Emergent rooted aquatic macrophytes-Vegetative vigor	Rice	Non-listed	EC_{25} > 886 ppm ae	467512-07
		Listed	NOAEC = 886 ppm ae (2% dry wt)	
Terrestrial plants-Seedling emergence	--	Non-listed	Data gap	--
		Listed	Data gap	--
Terrestrial plants-Vegetative vigor	--	Non-listed	Data gap	--
		Listed	Data gap	
Birds	Northern Bobwhite	Acute	LD_{50} = 885 mg ae/kg-bw[A]	425002-04
		Chronic	Data gap	--
Mammals	Rat	Acute	LD_{50} = 591 mg/kg-bw	433342-04
		Chronic	NOAEL >500 mg/kg/day	439288-01
Nontarget insects	Honeybee	Acute dermal (contact)	Data gap	--
		Acute oral	Data gap	--
		RT_{25}-wood preservative	Data gap	--

[A] Value shown is based on available data but there is a passerine species data gap.

4.4 Exposure Analysis Plan

The Agency lacks information on the fate profile for *o*PP with regard to the potential for biotic degradates/transformation products to be formed. Consequently, in the absence of information, the Agency will use a total toxic residue approach to determine potential toxicity to ecological organisms. This approach assumes any major degradates formed would be as toxic as the parent. The Agency will consider conducting a more refined risk assessment if information on the toxicity of any major degradates identified is provided.

4.4.1 Aquatic and Terrestrial Wildlife Exposure Estimates

4.4.1.1 Antimicrobial Use Patterns

Available OPP models that estimate exposures from both direct and indirect discharges to surface water (e.g., via a wastewater treatment plant) will be used to determine estimated environmental concentrations (EECs) in the aquatic environment. These exposure estimates will be compared to the toxicity endpoints to determine whether or not the Agency's levels of concern for acute and chronic risks to aquatic organisms, including listed species, are expected to be exceeded for each receptor group.

In the case of use patterns that result in antimicrobials entering surface water via indirect discharges to wastewater treatment facilities, the Agency will use a probabilistic approach that estimates the number of days of exceedance of concentrations of concern (COCs) for aquatic organisms located downstream of wastewater treatment plants. A more complete discussion of this approach as it relates to antimicrobials entering surface water via domestic wastewater treatment plants can be found in Appendix D. For those use patterns that result in antimicrobials entering surface water by way of industrial wastewater treatment plants, the Agency will use a different approach than that used for antimicrobials entering domestic wastewater treatment plants. The approach for assessing exposures for antimicrobials entering industrial wastewater treatment facilities relies upon estimating loadings of antimicrobials to industrial wastewater treatment plants and using the General Population Exposures from Industrial Releases module of E-FAST to estimate number of days of exceedance of COCs for aquatic organisms.

The tool used to predict EECs from leaching and subsequent transport to soil and potential run-off to surface water from antimicrobials in wood and materials preservatives is expected to be PRZM/EXAMS. A pervious soil, impervious surface, and a combination of pervious and impervious surfaces is expected to be used to bound risks.

4.4.1.2 Residential Insecticide Use Patterns

Stressors of Concern

Ecological Risk Assessment

Environmental fate data used to determine environmental degradates of *o*PP and its salts are lacking. Following receipt of anticipated data, the major degradates (>10%) will be identified and then screened via ECOSAR for toxicity to determine how they will be assessed in the registration review risk assessment. In the absence of additional data, the stressors of ecological concern for terrestrial and aquatic organisms are *o*PP and its salts.

Measures of Exposure

The Agency will use standard available models to evaluate potential exposures to aquatic and terrestrial organisms as described at http://www.epa.gov/pesticides/science/models_db.htm.

Screening level calculations have suggested that exposure via drinking water may be significant for terrestrial vertebrates (*i.e.*, birds and mammals). This exposure pathway may be further considered at the time of the risk assessment.

Available Monitoring Data

The Agency is aware of monitoring conducted by federal and state agencies, and this route of exposure will be considered in the assessment to the extent that data on *o*PP are available.

4.4.2 **Screening Level Down-the-Drain Analysis**

The Down-the-Drain (DtD) module of E-FAST (Exposure and Fate Assessment Screening Tool) was used to determine the potential for aquatic organisms downstream of domestic wastewater treatment plants (WWTPs) that receive discharges from application of *o*PP and salts to be exposed to *o*PP and salts and/or any degradates that form from the point of application to the point of discharge following wastewater treatment. The results of the DtD module runs are expressed as number or days of exceedance of concentrations of concern for aquatic organisms. A detailed description of derivation of data for input parameters selected to run the DtD module and of the theoretical basis for this model is presented in Appendix E. A conservative assumption of no removal during wastewater treatment was used in DtD model runs.

Table 14 presents high-end scenario results of a screening-level DtD analysis for *o*PP and salts based on laboratory toxicity data for freshwater organisms. Results are presented for a number of wastewater treatment plant influent volumes. Based on U.S. consumption in 2004 of 2,440,000 pounds and assuming an average annual volume growth of 2.5% per year, Kline (2004) predicted that in 2009 consumption of *o*PP and salts would be 2,760,000 pounds. This corresponds to about 1,250,000 kilograms of *o*PP and salts forecast to be consumed in 2009. In one scenario, it was assumed that all of the *o*PP and salts that was forecast to be consumed in 2009 would be discharged to domestic wastewater treatment plants. At this presumed wastewater treatment plant influent volume, COCs would be exceeded 3 days per year for endangered freshwater fish and 4 days per year for endangered freshwater invertebrates.

To exceed the concentration of concern of 430 ug/L for endangered freshwater algae for one day a year, it would take a wastewater treatment plant influent volume of *o*PP of about 2,225,000 kilograms per year. To exceed the acute concentration of concern of 1370 ug/L for freshwater fish for one day a year, it would take a wastewater treatment plant influent volume of about 7,500,000 kilograms per year. To exceed the acute concentrations of concern of 1255 ug/L for freshwater invertebrates and 1390 ug/L for freshwater algae for one day per year, it would take a wastewater treatment plant influent volume of about 7,000,000 kilograms per year.

Table 14 – Summary of Screening Level Down-the-Drain Analysis Results

Influent Volume of *o*PP	**Acute Freshwater Fish (COC = 1370 ug/L)**	**Endangered Freshwater Fish (COC = 137 ug/L)**
1,250,000 kilograms/year	No exceedance	Exceeded 3 days per year
2,225,000 kilograms/year	No exceedance	Exceeded 11 days per year
Influent Volume of *o*PP	**Acute Freshwater Invertebrates (COC = 1255 ug/L)**	**Endangered Freshwater Invertebrates (COC = 125.5 ug/L)**
1,250,000 kilograms/year	No exceedance	Exceeded 4 days per year
2,225,000 kilograms/year	No exceedances	Exceeded 13 days per year
Influent Volume of *o*PP	**Acute Freshwater Algae (COC = 1390 ug/L)**	**Endangered Freshwater Algae (COC = 430 ug/L)**
1,250,000 kilograms/year	No exceedance	No exceedance
2,225,000 kilograms/year	No exceedance	Exceeded 1 day per year
Influent Volume of *o*PP	**Acute Vascular Plants (COC = 6200 ug/L)**	**Endangered Vascular Plants (COC = 2300 ug/L)**
1,250,000 kilograms/year	No exceedance	No exceedance
2,225,000 kilograms/year	No exceedance	No exceedance

This screening level analysis assumes that *o*PP and salts are released to domestic wastewater treatment plants. Based on registered uses of *o*PP and salts presented in Table 6 of this FWP,

there are some uses, such as commercial and industrial cooling water systems and paper mill water systems, for which discharges may enter industrial WWTPs rather than domestic WWTPs prior to entering surface water. Different methods and tools for assessing potential exposures and associated ecological risks will be applied for these other types of uses.

There is considerable uncertainty regarding the amount of *o*PP and salts that could be expected to enter domestic wastewater treatment plants. There is also uncertainty about the potential for exposure to aquatic organisms from *o*PP and salts entering industrial wastewater treatment plants as a result of industrial uses of *o*PP and salts. Exceedances of concentrations of concern for endangered freshwater fish and invertebrates have been predicted at production volumes of *o*PP and salts projected by Kline for the year 2009 (Kline 2004), and there is evidence based on an evaluation of production data reported to the Agency that the Kline data tend to considerably underestimate the production volume of *o*PP and salts. The Agency does not have high quality data on the toxicity of *o*PP and salts to activated sludge microorganisms in wastewater treatment plants and does not have high quality data on biodegradation of *o*PP and salts during wastewater treatment. Consequently, the Agency anticipates needing the following data on *o*PP to fulfill data gaps regarding toxicity to activated sludge microorganisms and biodegradation of *o*PP and salts during wastewater treatment:

1. Activated Sludge Respiration Inhibition (OECD 209) or Modified Activated Sludge Respiration Inhibition (OCSPP 850.6800);
2. Ready biodegradability test (835.3110) or one of three biodegradation in activated sludge simulation tests (835.3220; 835.3280; 835.3240)

For more information on these tests, refer to Table 8.

4.5 Effects Analysis Plan

Toxicity data presented in this work plan will be used to calculate risk quotients and/or calculate COCs. Any additional information submitted by the registrant(s), other interested parties or found in the open literature prior to conduct of the risk assessment will also be considered. The open literature studies will be identified using EPA's ECOTOXicology (ECOTOX)[23] database, which employs a literature search engine for locating chemical toxicity data for aquatic life, terrestrial plants, and wildlife. The ECOTOX database will be searched when the risk assessment for *o*PP and salts is prepared. The evaluation of these sources of data can also provide insight into the direct and indirect effects of pesticides on biotic communities from loss of species that are sensitive to the chemicals and from changes in structure and functional characteristics of the affected communities.

5 Endocrine Disruptor Screening Program (EDSP)

As required by FIFRA and FFDCA, EPA reviews numerous studies to assess potential adverse outcomes from exposure to chemicals. Collectively, these studies include acute, subchronic and chronic toxicity, including assessments of carcinogenicity, neurotoxicity, developmental, reproductive, and general or systemic toxicity. These studies include endpoints which may be susceptible to endocrine influence, including effects on endocrine target organ histopathology, organ weights, estrus cyclicity, sexual maturation, fertility, pregnancy rates, reproductive loss, and sex ratios in offspring. For ecological hazard assessments, EPA evaluates acute tests and

[23] http://cfpub.epa.gov/ecotox

chronic studies that assess growth, developmental and reproductive effects in different taxonomic groups. As part of its reregistration decision, for *o*PP, EPA reviewed these data and selected the most sensitive endpoints for relevant risk assessment scenarios from the existing hazard database. However, as required by FFDCA section 408(p), *o*PP is subject to the endocrine screening part of the Endocrine Disruptor Screening Program (EDSP).

EPA has developed the EDSP to determine whether certain substances (including pesticide active and other ingredients) may have an effect in humans or wildlife similar to an effect produced by a "naturally occurring estrogen, or other such endocrine effects as the Administrator may designate." The EDSP employs a two-tiered approach to making the statutorily required determinations. Tier 1 consists of a battery of 11 screening assays to identify the potential of a chemical substance to interact with the estrogen, androgen, or thyroid (E, A, or T) hormonal systems. Chemicals that go through Tier 1 screening and are found to have the potential to interact with E, A, or T hormonal systems will proceed to the next stage of the EDSP where EPA will determine which, if any, of the Tier 2 tests are necessary based on the available data. Tier 2 testing is designed to identify any adverse endocrine-related effects caused by the substance, and establish a dose-response relationship between the dose and the E, A, or T effect.

Under FFDCA section 408(p), the agency must screen all pesticide chemicals. Between October 2009 and February 2010, EPA issued test orders/data call-ins for the first group of 67 chemicals, which contains 58 pesticide active ingredients and 9 inert ingredients. A second list of chemicals identified for EDSP screening was published on June 14, 2013[24] and includes some pesticides scheduled for registration review and chemicals found in water. Neither of these lists should be construed as a list of known or likely endocrine disruptors.

*o*PP is on List 1 for which EPA has received all the required Tier 1 assay data. The agency is currently reviewing all of the assay data received for the appropriate List 1 chemicals and planning to make the conclusions of those reviews available in early 2015. For further information on the status of the EDSP, the policies and procedures, the lists of chemicals, future lists, the test guidelines and the Tier 1 screening battery, please visit our website.[25]

6 Optional Label Changes

To eliminate the anticipated need for EPA to require certain data, reduce the possibility that EPA's planned risk assessments overestimate risk due to reliance on conservative assumptions, and/or improve label clarity, registrants may consider amending product labeling.

Some labels permit the use of handheld fogging. If the labels were amended to require that fogging be done only by automatic equipment, then EPA would likely no longer need the anticipated requirement for the indoor exposure study for handheld fogging.

All of the labels permit open pour addition of liquids and soluble powders for material preservation and industrial process treatment. If the labels were amended to require that liquids be handled using closed loading and delivery systems and that powders be packaged in water

[24] See http://www.regulations.gov/#!documentDetail;D=EPA-HQ-OPPT-2009-0477-0074 for the final second list of chemicals.

[25] http://www.epa.gov/endo/

soluble packaging, then EPA would likely no longer need the anticipated requirement for the indoor exposure study for open pouring of liquids and soluble powders.

7 Next Steps

A DCI will be developed regarding the data needs listed under the "Risk Assessments and Anticipated Data Needs" section of this document. The Agency expects to issue the DCI by March of 2015.

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Appendix A Toxicology Profile

The most recent review of the toxicity data for ortho phenyl phenol was included in the 2006 RED. No additional toxicology studies have been submitted to the Agency since publication of the RED, and no new toxicology studies are anticipated to be needed.

Acute Toxicity for Product Labeling

The acute toxicity database for *o*PP and salts shows that by the oral route, a Toxicity Category III is assigned based on results of two submitted studies (MRIDs 43334201 and 43334204) showing oral LD_{50} values of 2733 mg/kg (combined) and values of 846 and 591 mg/kg (males and females respectively). By the dermal route, an LD_{50} value of > 5000 mg/kg was obtained in a submitted study (MRID 00078779). In a submitted acute inhalation toxicity study (MRID 42333101), animals exposed nose-only to an aerosol of *o*PP (0.036 mg/L) showed no mortality; however, this study is currently not acceptable but could be upgraded if information is provided that an adequate (higher) atmospheric concentration of *o*PP could not be generated and that smaller particle sizes could not be achieved. A primary eye irritation study was conducted (MRID 00139884) but the study was considered unacceptable because the observation period employed in the study (7 days) was not long enough to assign a Toxicity Category. *Ortho*-phenyl phenol and its sodium salt are severe (Toxicity Category I) dermal irritants. *Ortho*-phenyl phenol and its sodium salt are not dermal sensitizers.

Table 15 – Acute Toxicity Studies for *o*PP

Guideline No./ Study Type	MRID No.	Results	Toxicity Category
870.1100/ Acute oral toxicity ***o*PP purity 99.9%**	43334201	LD_{50} = 2733 mg/kg	III
870.1100/ Acute oral toxicity **Na-*o*PP purity 99.1%**	43334204	LD_{50} = 846 mg/kg (male) LD_{50} = 591 mg/kg (female)	III
870.1200/ Acute dermal toxicity ***o*PP purity 99.73%**	00078779	LD_{50} > 5000 mg/kg	IV
870.1300/ Acute inhalation toxicity ***o*PP purity 99.9%**	42333101	Unacceptable study	NA
870.2400/ Acute eye irritation **Dowicide® 1**	00139884	Unacceptable study	NA
870.2500/ Acute dermal irritation ***o*PP purity 99.9%**	43334202	Primary Irritant	I
870.2600/ Skin sensitization ***o*PP purity 99.9%**	43334203	Not a sensitizer.	No
870.2600/ Skin sensitization **Na-*o*PP purity 99.1%**	43334205	Not a sensitizer.	No

N/A=Not available

Subchronic Toxicity

In a 90-day oral toxicity test (MRID 40760206) designed to determine the subchronic toxicity effects of repeated dietary exposure to *o*PP (>98% purity) in F344/DuCrj rats. *Ortho*-phenyl phenol was administered in feed to 10 rats/sex/dose at concentrations of 0, 0.156, 0.313, 0.625, 1.25, or 2.5% (0, 182, 391, 761, 1669, or 2798 mg/kg/day and 0, 202, 411, 803, 1650, or 3014 mg/kg/day for males and females, respectively) for 13 weeks. Animals were observed twice daily for changes in body weight and food and water consumption.

Mortality occurred in treated animals within 2 weeks of initiating the study, with death in 20% of males (4 days into study) and 10% of females (8 days into study) in the 2.5% dose group. Food consumption was slightly decreased in males and females of the 1.25% dose group. Males administered 2.5% *o*PP exhibited significant decreases from control in food intake. The discrepancy in food intake was greatest in the first week but decreased as the study progressed. Females of this group also exhibited a reduction in food consumption that was significantly less than the control until week 8; however, the decreased food intake trend continued throughout the remainder of the study. Additionally, the 2.5% rats spilled an excessive amount of feed at the initial stage of the study and they tended to be thin throughout the study period.

There were no other effects on food consumption in animals of the other dose levels except for males treated with 0.313% *o*PP. These rats showed significant increases in food consumption and food intake/body weight that appeared to be reflected in the body weight changes. Overall the feeding efficiency (increase in body weight over unit time in grams/feed intake in grams) was slightly lower in groups fed on feed containing high *o*PP concentrations.

Water consumption was significantly decreased from controls in the first week of the study in the 1.25 and 2.5% dose groups. There were no significant changes from controls in body weight gain in animals treated with *o*PP concentrations equal to or less than 0.625%. Weight gain was inhibited in males and females of the 1.25% dose group, with maximum inhibition ratios of 14 and 7%, respectively. The significant weight loss of 1.25% females occurred in the first 8 weeks of the study. Body weight gain was significantly reduced from controls in both male and female rats in the 2.5% *o*PP dose group.

The hemoglobin (Hgb) and mean red blood corpuscle hemoglobin concentration (MCHC) were significantly lower than controls in 1.25 and 2.5% females, while hematological analyses in the 2.5% males showed significant decreases from controls in red blood corpuscles (RBC), Hgb, and MCHC. There was a slight tendency for animals to be anemic in groups fed higher dosages of *o*PP. No treatment-related effects were observed in the serum analyses. Pathological and histological observations indicated treatment-related inflammation of the kidneys in both male and female rats (most pronounced in the 2.5% group) and abnormal growth in the mucous membrane of the male bladder (most pronounced in the 1.25% group).

The subchronic toxicity NOAEL is 0.625% (761 mg/kg/day, males; 803 mg/kg/day, females). The subchronic toxicity LOAEL is 1.25% (1669 mg/kg/day, males; 1650 mg/kg/day, females), based on significant reductions in body weight gain and food and water consumption.

In a 21-day dermal toxicity study (MRID 42881901) of systemic toxicity in Fischer 344 rats, male and female (5/sex/dose) were administered *o*PP (99.82% a.i.) over a 21 day study period for a total of 15 doses of 0, 100, 500, or 1000 mg/kg/day for 6 hours per day.

The highest dose tested, 1000 mg/kg/day, a limit dose for repeated dermal dosing regimens, produced no significant signs of systemic toxicity. Erythema and scaling was present in male and female rats at the 500 and 1000 mg/kg dose levels, with more severe irritation effects observed in the females. Microscopically, an increased incidence of acanthosis and hyperkeratosis was observed in male and female rats at the 500 and 1000 mg/kg dose levels.

The systemic toxicity NOAEL is greater than or equal to 1000 mg/kg/day (highest dose tested), and the systemic toxicity LOAEL is greater than 1000 mg/kg/day (not established). The dermal toxicity NOAEL is 100 mg/kg/day based on an increased incidence of dermal irritation reactions in male and female rats observed at the LOAEL of 500 mg/kg/day.

Developmental and Reproductive Toxicity

In a prenatal developmental toxicity study (MRID 92154037, reformat of 00067616 and 00164362), *o*PP (purity 99.69%) in cottonseed oil, was administered presumably by oral gavage (not specified) to groups of 37, 27, 27, and 26 rats/dose by gavage at dose levels of 0, 100, 300, or 700 mg/kg/day, respectively, from gestation days (GD) 6 to 15, inclusive. The animals were checked daily from gestation day 6 for indications of toxicity. Body weights were recorded daily from gestation days 6 through 15 and on gestation days 16 and 21. Food and water consumption were measured at 3 day intervals beginning on gestation day 6. Examinations at sacrifice consisted of a determination of the number and position of live, dead, and resorbed fetuses and staining of apparent nonpregnant uteri along with liver weights.

Minimal maternal toxicity was noted in the mid-dose group (91% of control) and greater maternal toxicity was noted in the high dose group (79% of control) during the dosing period as a decrease in body weight gain. Food consumption and food efficiency were slightly reduced in the mid and high dose groups during the dosing period. Also, the high dose group had reduced liver weights.

The maternal toxicity NOAEL is 100 mg/kg/day based on decreased body weight gains, food consumption and food efficiency. The maternal toxicity LOAEL is 300 mg/kg/day.

No developmental toxicity was noted at the dose levels tested. **The developmental toxicity NOAEL is greater than or equal to 700 mg/kg/day (highest dose tested). The developmental toxicity LOAEL is greater than 700 mg/kg/day (not established).**

In a prenatal developmental toxicity study in rabbits (MRID 41925001, 41925002, and 41925003), inseminated New Zealand White rabbits (7 females/group) were administered *o*PP (99.88% a.i.) on days 7-19 of presumed gestation by oral gavage at doses of 0, 25, 100, or 250 mg/kg/day. All animals were observed daily for signs of toxicity during the course of the study with body weights recorded on gestation days 0, 20, and 28 and then daily during the dosing period. Any animal that died or was sacrificed on study and all surviving animals at study termination were subjected to complete necropsy. Fetuses were examined for external, visceral, and skeletal alterations.

Administration of ortho-phenylphenol produced evidence of systemic toxicity at the 100 mg/kg/day (mid-dose) and 250 mg/kg/day (high-dose) levels. An increase in mortality occurred at the highest dose tested (three dams compared to one dam in the control group). Treatment-related alterations in microscopic kidney structure, primarily consisting of inflammation and tubular degeneration, were noted only in the high-dose animals. Observations of blood in the feces, urine, or cage pan was noted in the mid-dose (three dams compared to one control dam)

and high-dose (6 dams compared to one control dam) groups. Although the study author stated these effects to be of no toxicological significance because there was no correlation of these effects with signs of abortion and/or gross/microscopic pathologies, the EPA reviewer could not rule out this effect at the mid dose **The maternal toxicity NOAEL is 25 mg/kg/day and the maternal toxicity LOAEL is 100 mg/kg/day based upon increased incidence of blood in feces, urine, and/or cage pan.**

There were no statistically or biologically significant treatment-related differences in the incidence of fetal malformations or variations in any of the dose groups tested. Findings were sporadic, not dose-related and/or within the range of historical control data. **Therefore, the developmental toxicity NOAEL is greater than or equal to 250 mg/kg/day (highest dose tested) and the developmental LOAEL is greater than 250 mg/kg/day (not established).**

In a two-generation reproduction study (MRID 43928801) *o*PP (99+% a.i., Lot # PW08118LW) was administered to groups of 30 male and 30 female Sprague-Dawley rats in the diet at concentrations delivering doses of 0, 20, 100, or 500 mg/kg/day. Each group was administered the control or test diets continuously for 10 weeks prior to mating, during mating, gestation, and lactation through the production of two litters (F_{1a}, F_{1b}, F_{2a}, and F_{2b}) including a 14- or 20-day rest period after the first litters were weaned. The F_1 parents were selected when the pups were 21 days of age; the pups were weaned onto the same diets as received by their parents. The dietary concentrations were adjusted weekly based on the food consumption and body weight of the previous week to maintain a constant dose (mg/kg/day) except during gestation, lactation, and from weaning through week 3 of the premating period for F_1 pups. During these times, the animals received the same dietary concentrations of test material as the respective groups during the last week of the F_0 premating period.

No treatment-related effects were observed in male or female adult rats administered *o*PP at concentrations of 20 or 100 mg/kg/day. No treatment-related effects were observed on overall mortality, except for one F_0 male rat receiving 500 mg/kg/day that died due to kidney failure. The only treatment-related clinical sign of toxicity was urine staining in 5/30 ($p<0.05$) F_0 and 8/30 ($p=0.01$) F_1 males given 500 mg/kg/day compared with 0/30 for each control group. A 500 mg/kg/day, body weights at the end of the 70-day premating period were decreased by 2% (not significant) in F_0 males, 7% ($p<0.01$) in F_0 females, 11% ($p<0.01$) in F_1 males, and 9% ($p<0.01$) in F_1 females. At the end of the study (day 175), body weights were decreased by 5% (not significant) in the F_0 males and by 11% ($p<0.01$) in F_1 males administered 500 mg/kg/day. Corresponding reductions in weight gain during the 70-day premating period were -9 and -10% for F_0 and F_1 males and -19 and -8% for F_0 and F_1 females at 500 mg/kg/day compared with weight gain in the controls. Reductions in weight gain after 175 days of treatment were -19 and -10% in the F_0 and F_1 males. In contrast to weight gain, food consumption by males and females of both parental generations administered 500 mg/kg/day generally exceeded that of controls, and the F_1 dams weighed 6 to 8% less ($P<0.05$ or <0.01) than controls and the F_1 dams weighed 5% to 8% less (not significant, $p<0.05$ or $p<0.01$) than controls. Weight gain in 500 mg/kg/day group dams during gestation was similar to that of controls ranging from +1 to -7% of the control value for both parental generations; during lactation, weight gain for all treated groups in both generation ranged from -57 to +288% and showed no clear dose-related trends. For the first 124 days of lactation, food consumption in dams receiving 500 mg/kg/day ranged from 103 to 112% of the control values.

Urinary bladder calculi observed grossly (F_0: 4/30 vs. 0/30 for controls, not significant; F_1: 7/30 vs. 0/30 for controls, $P<0.05$) and microscopically (F_0 and F_1: 4/30 vs. 0/30, not significant) at 500 mg/kg/day in adult males were considered to be related to treatment with the test material. Wet/stained ventrum observed (F_0: 2/30 vs. 0/30 for control, not significant; F_1: 5/30 vs. 0/30 for controls, not significant) at 500 mg/kg/day in adult males was considered to be treatment-related. Other microscopic lesions attributed to treatment of male rats with 500 mg/kg/day of the test material included simple transitional cell hyperplasia (F_0: 22/30 vs. 1/30; F_1: 27/30 vs. 0/30; $p<0.05$), nodular/ papillary transitional cell hyperplasia of the urinary bladder (F_0: 16/30 vs. 1/30; F_1: 19/30 vs. 0/30; $p<0.05$) and chronic inflammation in the urinary bladder (F_0: 13/30 vs. 0/30; F_1: 12/30 vs. 0/30; $p<0.05$). The average severity ratings but not the incidences were significantly increased ($p<0.05$) for chronic inflammation in the kidney [F_0: 4/30 (2.8) vs. 0/30] debris in the renal pelvis [F_1: 4/30 (2.5) vs. 0/30], and dilation of the ureter [F_0: 4/30 (1.8) vs. 0/30]. No treatment-related pathologic lesions were observed in adult females.

No treatment-related effects on reproductive function or performance were observed in male or female rats of either generation. No treatment-related effects occurred on viability, clinical signs, litter size at birth, or at the end of lactation or sex ratio for the F_1 or F_2 pups. Body weights in 21-day old pups in the 500 mg/kg/day group were decreased significantly ($p<0.01$) in both litters of each generation (-10 to -12%). F_{2b} pups at 500 mg/kg/day weighed 7% less ($p<0.05$) than controls on day 14 of lactation; no other statistically significant effects on pup weights were observed. Pup weight gain at 500 mg/kg/day was reduced by 12 to 14% over the entire lactation period. The reduced pup weights and weight gain is not attributed to lactational effects in the dams, but is considered to be related to consumption of the treated food.

The parental toxicity LOAEL is 500 mg/kg/day in males and females, based on reduced body weight and body weight gain in the adults, reduced body weight in 21-day old pups, clinical signs in adult male rats, microscopic lesions in the kidneys, and gross and microscopic lesions in the urinary bladder of adult male rats, and the death of one adult male rat due to kidney failure. The parental toxicity NOAEL is 100 mg/kg/day. No treatment-related reproductive toxicity occurred in male or female rats; therefore the reproductive NOAEL is >500 mg/kg/day.

Chronic Toxicity and Carcinogenicity

Combined chronic toxicity / Carcinogenicity – Rat

In a combined chronic toxicity /carcinogenicity study (MRID 43954301) CDF rats from SASCO, Inc., Madison WI received *o*PP (99.5—100% a.i.; Batch # S-01-93, Mixture of Bayer AG, Leverkusen, Germany and Dow, Midland, Michigan) in the diet for 24 months at dose levels of 0, 800, 4000 and 8000 ppm in males, and 0, 800, 4000, and 10000 ppm in females (39, 200, and 402 mg/kg/day for males for the 800, 4000, and 8000 ppm dose groups and 49, 248, and 647 mg/kg/day for females fat: the 800, 4000, and 10000 ppm dose groups). Interim sacrifice groups of twenty animals/sex for control and high dose groups and ten animals/sex for low and mid dose groups were sacrificed at 12 months. Systemic toxicity was noted as decreased body weights ($p < 0.05$) and body weight gains in both males and females of the mid and high dose groups during the first 13 weeks of- the study (for the 2-year carcinogenicity group). At study termination, only the high dose groups had reduced body weights ($p < 0.05$) and body weight gains. Food consumption was slightly decreased in the 2- year carcinogenicity group in the high dose group at all time points measured and was decreased in the mid dose females at 13 weeks. Food

efficiency determined for the first 13 weeks was slightly decreased in the mid dose group and greatly decreased in the high dose, group. There was an increase in observed masses in the urinary bladder of high dose males at 24 months. High dose females had an increased incidence of kidneys with pitted zones at 24 months. Mid and high dose females had an increase in wet/stained ventrum at 12 months and both high dose males and females had a similar observation at 24 months, this was attributed to the urine and red staining in the perigenital area noted in the clinical observation data. Non-neoplastic observations noted an increase in incidence of calculus in the kidneys in high dose males at the 12 month sacrifice and the 24 month study termination. There was also increased hyperplasia of the urinary bladder at 12 and 24 months in high dose males (and high dose females at 24 months) along with an increase in congestion, hemorrhage, mineralization and necrosis of the urinary bladder at 24 months in high dose males. High dose males and females also had an increase in cysts of the kidney at 24 months. High dose females had an increase in hyperplasia of the kidney along with increased infarct, acute inflammation and mineralization of the kidney. **Based on the results of this study, the Systemic Toxicity NOEL is equal to 800 ppm (39 mg/kg/day for males and 49 mg/kg/day for females and the Systemic Toxicity LOEL is equal to 4000 ppm (200 mg/kg/day for males and 248 mg/kg/day for females) based on decreased body weight gains, decreased food consumption and reduced food efficiency, and increased clinical and gross pathological signs of toxicity.**

This study is classified as **Acceptable – Guideline**.

In a carcinogenicity study (MRID# 43545501) B6C3F1 albino mice (50/sex/dose group) from Charles River Laboratory, Portage, MI received ortho-phenylphenol (99.88% a.i.; Lot# 8800005-24, mixture of Dow Chemical Company and Miles, Inc. products) in the diet for 24 months at dose levels of 0 250, 500 and 1000 Mg/kg/day. A satellite group of ten animals/sex/dose group were sacrificed at 12 months.

Systemic toxicity was noted in treated females at 3 months as decreased body weight gain (10-12%), statistically significant but not dose related. At 12 and 24 months there was a 14-25% decrease in body weight gain in males and females of the mid dose and a 27-38% decrease in the high dose groups. Treated females had slightly reduced food consumption during the first 90 days. Food efficiency for this period was slightly reduced for the male dose groups and variable for the female dosed groups (no dose response effect). At 1 year there was no treatment related effects on food consumption and at 2 years there was a slight increase in food consumption in all treated groups. There was an increase in absolute and relative liver weights at 12 and 24 months in all treated males and females; also, treated males had increased adrenal absolute and relative weights at 24 months. Spleen weights (absolute and relative) in the males and females were reduced in all treated groups. **The Systemic Toxicity LOEL is less than or equal to 250 mg/kg/day and the Systemic Toxicity NOEL lees than 250 mg/kg/day based on increased liver and reduced spleen weights and gross observations in the liver of all treated animals**

This study is classified as Core-Minimum data and satisfies the guideline requirement (83-2b) for a carcinogenicity study in the mouse.

Mutagenicity

An analysis of the genetic toxicology data from over 130 studies with *o*PP was undertaken by Brusick (2005) who found that there was no indication of gene mutations in bacteria or in mammalian cells such as Chinese hamster ovary (CHO) cells and that positive results with mouse lymphoma ($Tk^{+/-}$) were generally associated with cytotoxicity. Similarly, clastogenicity,

which was the most frequently observed type of genotoxicity, was consistently linked with cytotoxicity. For *o*PP, the most common type of structural chromosome damage was chromosome breaks, an event that Brusick describes as typically resulting in cell death. Mixed results were found in studies assessing direct interaction with DNA damage. Based on the weight-of -the-evidence analysis, it was concluded that positive findings in genetic toxicology tests were related to 'excessive cytotoxicity, not direct DNA damage". Furthermore, Brusick (2005) states that agents that shift the normal cellular antioxidative balance and induce cytotoxicity are considered threshold-dependent because exposure levels that do not produce alterations in homeostais do not produce DNA damage (i.e., genotoxicity). In other words, oxidative damage, eventually leading to cell lethality, only occurs at concentrations that have exceeded the levels that can be handled by normal homeostasis. This observation is supported by the analysis of the carcinogenic mechanism of 2-phenylphenate by Niho *et al*. (2002). From the dose- and time-response studies with *o*PP and urinary bladder carcinogenicity in rats, investigators found that the tumor induction was a high-dose phenomenon, producing a steep dose response at 15,000 and 20,000 ppm but negative at 10,000 ppm. Similarly, a steep time response curve was plotted with transitional cell carcinoma development only seen in 4% of the animals after 24 weeks of continuous oral exposure but increasing dramatically after 24 (53%) and 52 (71%) weeks. The non-linearity of this response suggested to the authors that the tumor response observed in these studies with *o*PP is consistent with a threshold effect.

Metabolism and Pharmacokinetics

The metabolism and pharmacokinetics of ortho-phenylphenol have been examined in studies from the peer reviewed scientific literature (Reitz *et al*., 1983; Bartels *et al*., 1998). An oral dose of ortho-phenylphenol can be directly conjugated with glucuronic acid or sulfate to form the glucuronide and sulfate conjugate or can be metabolized by cytochrome P-450 isozymes to form hydroxylated metabolites (phenylhydroquinone and 2,4 dihydroxybiphenyl) which are then in turn conjugated with glucuronic acid or sulfate. At doses below approximately 200 mg/kg, ortho-phenylphenol is found primarily in urine as the glucuronide and sulfate conjugates in both rats and mice. With increasing dose, however, the metabolic profile changes and this has been postulated to be related to the carcinogenic mode of action for ortho-phenylphenol. Briefly, Biotransformation of *o*PP initially involves formation of phenolic metabolites (such as 2,4'-dihydroxyphenyl and phenylhydroquinone) in the liver through the action of cytochrome P-450 (demonstrated by Ozawa *et al*. [Xenobiotica 30(10), 1005-1017, 2000], by rat CYP2C11 and possibly CYP2E1, and human CYP1A2. *Ortho*-phenyl phenol, phenylhydroquinone, and 2,4'-dihydroxybiphenyl can themselves undergo conjugation reactions through the action of either sulfotransferase or glucuronidation phase II reactions. Phenylhydroquinone can also be converted to phenyl-1,4-benzoquinone by a secondary peroxidase-mediated activation in the kidney and/or bladder involving the prostaglandin endoperoxide synthase (PHS) complex. The involvement of PHS has been suggested on the basis of data submitted to the Agency (D203250), where in vitro incubations were conducted with microsomal PHS from ram seminal vesicles using *o*PP or the metabolites phenylhydroquinone (PHQ) and phenylbenzquinone (PBQ). This study demonstrated a role for PHS in conversion of PHQ to PBQ.

The presence of PHS in the bladder epithelium has been proposed by Kolachana *et al*. (Carcinogenesis 12(1): 145-149, 1991) as possibly responsible for the activation of PHQ to reactive intermediates in the bladder and kidney**.** The generation of PBQ is considered dose-dependent, appearing in increased quantity only at higher (>200 mg/kg/day) doses of *o*PP. The

shift in biotransformation products with increased dose of *o*PP has been postulated to be associated with the non-linear response observed in tumorigenicity of the urinary bladder and liver, involving oxidative damage to cells and subsequent regenerative hyperplasia. With continued exposure, this process leads to development of tumors.

Dermal Absorption

Dermal Absorption Factor: The Agency has not received any animal studies on the magnitude of dermal absorption of *o*PP. In the absence of these data, the Agency expects to use a default value of 100% for dermal absorption until such time that an acceptable dermal absorption study in animals is available.

Classification of Carcinogenic Potential

In accordance with the EPA Final Guidelines for Carcinogen Risk Assessment (March 29, 2005), the CARC classified *o*PP as "Not Likely to be Carcinogenic to Humans" based on convincing evidence that a non-linear mode of action for bladder tumors was established in rats. High doses of *o*PP lead to saturation of phase II detoxification enzyme pathways, resulting in increased amounts of the oxidative metabolites PHQ and/or PBQ. The generation of PBQ is considered dose-dependent, appearing in increased quantity only at higher doses of *o*PP (>200 mg/kg/day). The shift in biotransformation products with increased dose of *o*PP has been postulated to be associated with the non-linear response observed in tumorigenicity of the urinary bladder, involving oxidative damage to cells and subsequent regenerative hyperplasia. With continued exposure, this process leads to development of tumors. Evidence suggests that there are not sufficient oxidative metabolites generated in vivo to result in a genotoxic mode of action, but that a non-genotoxic mode of action is operative.

Although there is some mode of action data for the mouse liver tumors, the nature of these tumors and their response (benign tumors in one sex at the limit dose and one-half the limit dose in a susceptible strain) would not be the basis for quantification of human risk. However, data do suggest that this tumor type may also arise from a non-linear mode of action.

In addition, the non-cancer assessment for *o*PP established a chronic Reference Dose value of 39 mg/kg/day from the combined chronic toxicity/carcinogenicity study in rats (MRIDs 43954301, 44852701, 44832201) based on decreased body weight gains, decreased food consumption and reduced food efficiency, and increased clinical and gross pathological signs of toxicity at the LOAEL of 200 mg/kg/day. The selection of 39 mg/kg/day as the chronic RfD value is sufficiently protective of the key events involved in the carcinogenic mode of action, which are not present at doses below 200 mg/kg/day. Thus, the precursor events leading to development of bladder and liver tumors are not likely to occur using the selected chronic RfD value and this value is thus protective against development of tumors and, therefore, cancer is not an issue.

Immunotoxicity

An immunotoxicity study is a data requirement for all antimicrobial pesticide chemicals under 40 CFR Part 158W, Data Requirements for Antimicrobial Pesticides. The registrant can address this data requirement by either submitting a study according to the OCSPP 870.7800 guideline, or by submitting a request for waiver of this study using the Agency's published guidance, available at: http://www.epa.gov/pesticides/regulating/part158-tox-data-requirement.pdf.

Appendix B Environmental Fate

EPA completed a RED on 2-Phenylphenol and sodium salt or *ortho*-phenylphenol and sodium salt in 2006 for the then registered antimicrobial use sites. In the present registration review document, the Agency has taken into account EPA's RED assessment but also has identified additional exposure scenarios that were not considered in the 2006 RED.

A number of risk assessments documents, including environmental fate and transport for these chemicals, have been completed by various organizations either before, during or after the Agency's RED publication. These include: PMRA of Canada[1] (2008), IRIS[2], FAO[3] (1999), and CalEPA[4], Department of Pesticide Regulation (2007): Risk Characterization Document.

Ortho-phenyl phenol is a weak acid with a pKa of about 9.95 at 25°C (MRID 41605001), indicating that *o*PP will in aqueous solution primarily exist as the protonated acid at environmental pH values (5 - 9). In solution, the sodium (Na) and potassium (K) salts of *o*PP rapidly dissociate releasing sodium and potassium cations (Na^+ and K^+, respectively) and the *ortho*-phenyl phenate anion (oPP^-). Depending on the pH of the solution the oPP^- anion will readily become protonated forming the neutral or unionized *o*PP or will readily release a proton to form the oPP^- anion. The equilibrium in solution between oPP^- and protonated or unionized *o*PP depends on the pH of the solution. Therefore, the fate and transport data supporting *o*PP can be used to support the salts and similarly the fate and transport data supporting its Na and K salts may be used to support *o*PP.

Ortho-phenyl phenol is hydrolytically stable under abiotic conditions. It does photodegrade in abiotic aqueous medium forming three degradates. It is immobile on surfaces and will not contaminate the ground water. It is ready biodegradable. It has a high log K_{ow} indicating it is potentially bioaccumulative; however, there is no data on bioaccumulation or bioconcentration in aquatic organisms.

Na-*o*PP is applied to and leaches out easily from sapstain treatment on wood surfaces, and almost 75% is eliminated from wood surfaces within 14 days. Since Na-*o*PP ionizes in moist soils, it is more likely to be mobile from such soil surfaces.

Abiotic Degradation of *o*PP

Ortho-phenyl phenol is hydrolytically stable under abiotic conditions at pH 5, 7, and 9 (MRID 439942-01); however it degrades photolytically when exposed to sunlight under neutral conditions. Exposure to ultraviolet (UV) light (257.7 nanometers (nm)) degrades *o*PP to form: phenylbenzoquinone (PBQ), phenylhydroquinone (PHQ) and 2-hydroxy benzofuran (MRID# 439942-01).

The half life of *o*PP in air is estimated at 14 hours (measured against the hydroxyl radical) (EPI Suit, version 4.1). Therefore, it is considered moderately stable in air. Its estimated K_{oc} value of 10,000 (EPISuite, version 4.1) indicates it is immobile in soils and shows no tendency to migrate into soils. It likely will not contaminate ground water.

Biotic Degradation of *o*PP

The half life of *o*PP in air is estimated to be 0.03 hours using EPISuite 4.10. A study report of Wick and Gschwend (1998a) on surface water showed the degradation rates of *o*PP ranged from 16.5 to 38.4 hours in spring, summer, and fall seasons, but did not show any degradation in the

winter season. In a study using river water, Gonsior (1984) indicates that the half life of *o*PP is about 168 hours (7 days). Zbozinek (1984) studied microbial degradation of *o*PP in soil with half-lives ranging from 24 to 168 hours. None of these studies were of ultimate biodegradation or mineralization and also did not identify degradates.

The river water study by Gonsior (1984) used water from Tittabawassee River in Midland, Michigan and carbon-14 (^{14}C) radio-labeled *o*PP. A 50% reduction of ^{14}C labeled *o*PP occurred within a week. After 16 days, carbon dioxide containing ^{14}C ($^{14}CO_2$) reached the levels of 50%, 65% and 50% from the radiolabeled *o*PP samples of 1.22, 12.3 and 123 µg/L. The results are indicative of mineralization and ready biodegradability of oPP.

Gonsior (1984) also conducted a biodegradation study on an activated sludge with ^{14}C-labeled *o*PP. The biodegradation process of radio-labeled *o*PP was examined with non-acclimated and acclimated activated sludge, which was obtained from East Lansing, MI. A 50% reduction of radiolabeled *o*PP was observed within 24 hours and 3 hours in non-acclimated and acclimated sludge respectively. Thus if oPP is adsorbed on activated sludge, it is ready biodegradable from such surfaces. The recovery of total radioactivity in non-acclimated sludge ranged from 90- to 117%, and 78-100% for the acclimated sludge.

In another lake study (Wick and Gschwend 1998) the biodegradation of *o*PP was conducted using a mixture of diphenyl sulfone, *o*PP, and *para*-phenylphenol (*p*PP) at respective concentrations of 45, 100, and 230 µg/L quantities entering into a lake in Woburn Massachusetts. The lake was located at a ground water discharge from a Superfund Site. All three substances readily biodegraded during the summer months, with less biodegradation occurring during the fall and almost none in the winter months.

A more recent study (Tajeddine *et al*. 2010) on the photodegradation of *o*PP, and monuron, when placed on potassium- (K-) and iron (III)- (Fe(III))-monomorillonite clays showed that *o*PP degraded with a first order half life of 2 hours 3 minutes for K-montmorillonite, and 4 hours 18 minutes for Fe(III) monotmorillonite clay. Photodegradation experiments were conducted in a photoreactor (Suntest) which provided the simulated sunlight. The study is a non-guideline study and the results are indicated of biodegradation tendency of *o*PP, Na-*o*PP, and K-*o*PP on various types of soil surfaces.

Bioaccumulation of *o*PP

The Log K_{ow} of 3.09 to 3.36 for *o*PP has been reported. This chemical is likely to be bioaccumulative. No concrete data on bioaccumulation or bioconcentration into aquatic organisms has been reported.

Leaching of Na-*o*PP from Treated Wood

Na-*o*PP is used for sapstain treatment on woods. Leaching rates are reported from a study submitted by the registrants ((A Memo (Sept., 2005) from Najm Shamim, Chemist to Ben Chambliss, Team Leader in RMB2, MRID # 46601401)) where 1% and 4% solution of Na-*o*PP were applied as sapstain on wooden blocks. 1 % treated samples leached 52% of the active within the first day; 4% treated wood leached 58% of the active, and by day 14, 72-78 % of the active leaches out. The leach rate for 1% treated wood was: 71 µg of Na-*o*PP/cm^2 /day and for 4% treated wood the leach rate was: 192 µg of Na-*o*PP /cm^2 /day; after day 14, the leach rate was: 0.5 to 0.2 µg /cm^2/day for both treated woods. At the end of the study, 20-24% of Na-*o*PP was extracted from the wooden blocks.

Degradates of *o*PP

The Agency has used its internal database EPI Suite, version 4.1 to estimate physical/chemical as well as some environmental fate characteristics for the degradates PBQ and PHQ.

Environmental Fate of the Photo-Degradates: PHQ and PBQ

PHQ

The estimated data on this compound (EPI Suite, version 4.1) indicates that this substance is highly water soluble, and its vapor pressure is not of concern for exposure assessment. Its estimated half life is 15 days in water bodies, and about thirty days in soils, making it not persistent in these environmental media. It could be stable and persistent in sediments with an estimated half life of 135 days. It is not stable in air and the estimated half life is less than six hours in air. It is not likely to be bioaccumulative as its log K_{ow} is less than 3. It appears to be not readily biodegradable and may not be removed from the wastewater treatment plants. But with the half life of 15 days in water bodies, it may not reach the wastewater treatment plants. It has a high K_{oc} value making it immobile in soils, thus the probability of this chemical migrating to ground water is low and so ground water contamination is not likely to happen.

PBQ

The estimated data on this compound (EPI Suite, version 4.1) indicates that this substance is highly water soluble, and its vapor pressure is not of concern for exposure assessment. Its estimated half life is 15 days in water bodies, and about thirty days in soils, making it not persistent in these environmental media. It could be stable and persistent in sediments with an estimated half life of 135 days. It is not stable in air and the estimated half life is less than eight hours in air. It is not likely to be bioaccumulative as its log K_{ow} is less than 2. It appears to be not readily biodegradable and may not be removed from the wastewater treatment plants. It has a high K_{oc} value making it immobile in soils, thus the probability of this chemical migrating to ground water is low and so ground water contamination is not likely to happen.

Table 16 – Key Physical-Chemical Properties and Environmental Fate Characteristics of *o*PP and its Salts

Property/Study	*o*PP and its Salts	Remarks/Conclusions
Vapor pressure	*o*PP: Na-*o*PP	MRID 42441702, 41609505, The studies were acceptable and fulfill the date requirements
Log Kow	*o*PP:3.09-3.36	
Log Koc	*o*PP: 10,000 (EPI Suite, version 4.1)	Immobile in soils; will not contaminate ground water
Solubility		
Acid dissociation constant pKa	9.2	MRID 42441703, 42500202
Hydrolysis	Hydrolytically stable at pH 5, 7, and 9 (*o*PP);	MRID 43973501, 43994201
Aqueous photodegradation	A study with *o*PP was conducted at pH 7. Photodegrades in aquatic medium forming the degradates: PBQ, PHQ and 2-hydroxybenzofuran. The PBQ and PHQ are major degradates. Half-life n water both have half life of 15 days; in soil, both have half life of 30 days (EPI Suite, version 4.1)	MRID 43973501 The half lives for PBQ and PHQ are provided as estimates from EPI Suite (version 4.1); the study itself did not provide the half lives of the degradates.
Air stability/persistence in air	Is not stable or persistent in air; Half life in air: 14 hours	EPI Suite v4.1

Property/Study	*o*PP and its Salts	Remarks/Conclusions
Soil photodegradation	Photodegradation is fast for *o*PP in this type of soil *o*PP: Under simulated sunlight in K-Monomorillonite: half-life 3 hours 2 minutes; in Fe(III)-monomorillonite: half-life 4 hours and 18 minutes. Major degradates: the study did not identify the degradates	Arabian Journal of Chemistry, 2010, volume 3, pp 73-78)./ Non-guideline study, Supplemental
Aerobic Aquatic Metabolism	River study: Samples from Tattabawsee river in Midland MI, were treated with *o*PP (1.26, 12.6 and 126 microgram level. *Ortho*-phenyl phenol was radiolabeled: 50% degradation in seven days, and 50, 65, and 50% degradation in sixteen days. Lake Study: Mixture of diphenyl sulfone, *o*PP, and *para*-phenylphenol: Ready biodegradable in during summer months, less in fall, and none in winter months. Major degradates: Not reported.	*Ortho*-phenyl phenol is Ready biodegradable (Gonsoir *et al.* study: 1984, J. Agr. Food Chemistry, volume 32, pp 593-596; Activated sludge; same study (Gonsoir *et al.*) Non-guideline study; supplemental Biodegradability dependent on seasons. Warmer months accelerate biodegradation, cooler months make it less likely (Wick *et al.*, 1998, Environ. Sci. Technol., volume 32, pp 1319-1328) Non-guideline study
Activated sludge study	Ready biodegradable in the activated sludge. Activated sludge study: non-acclimated sludge: half life of radiolabeled *o*PP: 24 hours; acclimated sludge: radiolabeled: half life 3 hours. The sludge was obtained from East Lansing, MI. Major degradates: Not provided	Non-guideline study MRID 46359.
Leaching from sapstain treated wood	Sapstain leaching: 1% treated wood: 52% first day; 4% treated sapstain wood: 58% first day. 72-78% by day 14; Rate of leaching: 1%: treated wood: 71 µg /cm^2/day Rate of leaching: 4% treated wood: 192 µg /cm^2/day; rate of leaching after 14 days: 0.5 to 0.2 µg /cm^2/day for both treated wood. The sapstain study was conducted on Na-*o*PP.	Na-*o*PP was chosen to increase water solubility; rate of leaching is high AD (Memo by Najm Shamim to Ben Chambliss, September, 2005.(MRID# 466014-01) The study was a guideline study (based on Canadian guidelines, conducted by Dow Chemical Company, Study ID#: 051089, and DP Barcode: 319656The results show a very high leaching rate, and an equilibrium is reached within fourteen days.
Key Degradates:	phenylbenzoquinone (PBQ), phenylhydroquinone (PHQ)	No experimental fate data is available for these degradates.

The table below lists physical/chemical and environmental fate characteristics of: phenylbenzoquinone (PBQ) and phenylhydroquinone (PHQ) (EPI Suite, version 4.1, accessed on April 12, 2012)

Table 17 – Physical/Chemical and Environmental Fate Characteristics of PBQ and PHQ

Property	1,1-Biphenyl-2,5-diol	2,5-Cyclohexadiene-1,4-dione-2-phenyl	Source
Common Name	Phenylhydroquinone (PHQ)	Phenylbenzoquinone (PBQ)	EPI Suite (version 4.1)
CAS #	1079-21-6	363-03-1	EPI Suite (version 4.1)
MF/MW	$C_{12}H_{10}O_2$ / 186.21	$C_{12}H_8O_2$ /184.20	EPI Suite (version 4.1)
MP	126.99 ° C	100.07 ° C	EPI Suite (version 4.1)

Property	1,1-Biphenyl-2,5-diol	2,5-Cyclohexadiene-1,4-dione-2-phenyl	Source
VP	3.57 x10^{-5} mm Hg	9.23 x10^{-5} mm Hg	EPI Suite (version 4.1)
Solubility	798.2 mg/L	1135 mg/L	EPI Suite (version 4.1)
K_{ow}	2.80	1.95	EPI Suite (version 4.1)
Ready Biodegradability	NO	NO	EPI Suite (version 4.1)
STP	4.31% removal in wastewater treatment plant	2.20% removal in wastewater treatment plant	EPI Suite (version 4.1)
Half life in Air	5.897 hours (against OH radical)	7.137 hours	EPI Suite (version 4.1)
K_{oc}	8634 L/kg	800.8 L/kg	EPI Suite (version 4.1)
Half life in water	360 hours (15 days)	360 hours (15 days)	EPI Suite (version 4.1)
Half life in soil	720 hours (30 days)	720 hours (30 days)	EPI Suite (version 4.1)
Half life in sediment	3240 hours (135 days)	3240 hours (135 days)	EPI Suite (version 4.1)

Note: These two degradates are also detected in the mammalian toxicity (metabolism) study as discussed in the Health assessment section of this document.

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Appendix C Ecotoxicology Profile

Toxicity to Terrestrial Receptors

Birds

Available acute oral studies categorize *o*PP and salts as being slightly to practically nontoxic to birds (Table 18). Neither acute oral data with a passerine species, nor chronic data have been submitted. Therefore, guidelines 850.2100and 850.2300) are expected to be required.

Table 18 – Avian Toxicity Data

Test Species	Test Material (% a.i.)	Toxicity[26]	Toxicity Category	MRID/ Study Classification
Mallard (*Anas platyrhynchos*)	*o*PP (99.2)	LD_{50} > 2250 mg ae/kg-bw NOAEL ≥ 2250 mg ae/kg-bw, no mortality or body weight gain effect	Practically nontoxic	00160150/ Acceptable
Northern bobwhite (*Colinus virginianus*)	Na-*o*PP (75.9)[27]	LD_{50} = 885 mg ae/kg-bw (1000 mg a.i./kg-bw) NOAEL = 55.3 mg ae/kg-diet (62.5 mg a.i./kg-diet)	Slightly toxic	42500204/ Acceptable
Mallard (*Anas platyrhynchos*)	*o*PP (99.2)	LC_{50} > 5620 mg ae/kg-diet NOAEC = 3160 ae/kg-diet, reduction in body weight gain	Practically nontoxic	160151/ Acceptable
Mallard (*Anas platyrhynchos*)	Na-*o*PP (75.9)[27]	LC_{50} > 4980 mg ae/kg-diet (>5620 mg a.i./kg-diet) NOAEC = 1580 mg ae/kg-diet (1780 mg a.i./kg-diet), reduction in body weight gain	Practically nontoxic	42500206/ Acceptable
Northern bobwhite (*Colinus virginianus*)	*o*PP (99.2)	LC_{50} > 5620 mg ae/kg-diet NOAEC ≥ 5620 ae/kg-diet, no mortality or reduction in body weight gain	Practically nontoxic	160149/ Acceptable
Northern bobwhite (*Colinus virginianus*)	Na-*o*PP (75.9)[27]	LC_{50} > 4980 mg ae/kg-diet (>5620 mg a.i./kg-diet) NOAEC = 1580 mg ae/kg-diet (1780 mg a.i./kg-diet), reduction in body weight gain	Practically nontoxic	42500205/ Acceptable

Nontarget Insects

Nontarget insect toxicity data (850.3020, 850.3030) are expected to be required to support the assessment of the wood preservative use of *o*PP and salts.

[26] For *o*PP mg a.i. is equal to mg acid equivalent (ae), whereas mg a.i. of Na-*o*PP were converted to mg ae by multiplying by the molar weight ratio of *o*PP to Na-*o*PP (170.2/192.19 = 0.886).

[27] The test substance is actually sodium *ortho*-phenylphenate tetrahydrate (Na-*o*PP·$4H_2O$) but is represented in the table as Na-*o*PP without the weight percent of water. With the weight percent of water added, the purity of the test substance is >99%.

Toxicity to Aquatic Receptors

Freshwater Fish

The available acute toxicity studies (850.1075) categorize *o*PP and salts as being moderately toxic to freshwater fish (Table 19). The guideline (850.1075) for acute toxicity testing is satisfied. Chronic data (fish early-life stage, 850.1400) are expected to be required.

Table 19 – Freshwater Fish Toxicity Data

Species, Age or size	Test Material (% a.i.)	Exposure Type/ pH/ hardness[28]/ temperature	Toxicity Endpoint[29]	Toxicity Category	MRID/ Study Classification/ Comments
Rainbow trout (*Oncorhynchus mykiss*)	Na-*o*PP (71.48%)	Flow-through	--	--	46751206/ Unacceptable Percent recoveries were below acceptable range
Rainbow trout (*Oncorhynchus mykiss*), 1.1 g	*o*PP (95%)	Static/ 7.1/ 35/ 10±1 °C	96-h LC_{50} = 2.75 ppm ae 95% CI = 2.4-3.2 ppm ae Probit slope = NA NOAEC = 2.4 ppm ae, mortality, loss of equilibrium, dark coloration	Moderately toxic	110232/ Supplemental/ Solvent concentration used unknown
Rainbow trout (*Oncorhynchus mykiss*), 0.21 g, 2.8 cm SL	*o*PP (99.25%)	Static/ 7.4-8.2/ 78/ 12.1-12.5 °C	96-h LC_{50} = 4.0 ppm ae 95% CI = 3.6-4.5 ppm ae Probit slope = NA NOAEC = 1.8 ppm ae, immobilization, melanized fish	Moderately toxic	156044/ Acceptable
Bluegill sunfish (*Lepomis macrochirus*)	Na-*o*PP (71.48%)	Flow-through	--	--	46751210 Unacceptable Percent recoveries were below acceptable range
Bluegill sunfish (*Lepomis macrochirus*), 1.0 g	*o*PP (95%)	Static/ 7.1/ 35/ 20±1 °C	96-hr LC_{50} = 2.74 ppm ae 95% CI = 2.4-3.1 ppm ae Probit slope = 12.09 NOAEC = 1.0 ppm ae, loss of equilibrium, dark coloration	Moderately toxic	110232/ Supplemental/ Solvent concentration used unknown
Bluegill sunfish (*Lepomis macrochirus*), 0.4 g, 37.9 mm	Na-*o*PP·$4H_20$ (97%)	Static/ 7.0/ 51.3/ 18.3 °C	96-h LC_{50} = 3.9 ppm ae (6.1 ppm ts) Probit slope = NA	Moderately toxic	110135 (TN 640), 110203/ Supplemental

[28] As mg/L calcium carbonate ($CaCO_3$).

[29] For *o*PP mg a.i. is equal to mg ae, whereas mg a.i. of tests expressed as Na-oPP where converted to mg ae by multiplying by the molar ratio of oPP to Na-oPP (170.2/192.19 = 0.886) and results expressed as the tetrahydrate sodium salt (Na-*o*PP·$4H_20$) were converted to mg ae by multiplying by the molar weight ratio of *o*PP to Na-*o*PP·$4H_20$ (170.2/264.28 = 0.664).

Species, Age or size	Test Material (% a.i.)	Exposure Type/ pH/ hardness[28]/ temperature	Toxicity Endpoint[29]	Toxicity Category	MRID/ Study Classification/ Comments
Bluegill sunfish (*Lepomis macrochirus*), 0.15 g, 2.0 cm SL	*o*PP 99.25%	Static/ 7.5-7.9/ 77/ 17.1-17.4 ºC	96-h LC_{50} = 4.6 ppm ae 95% CI = 4.4-4.8 ppm ae Probit slope = 31.1 NOAEC = 3.2 ppm ae, immobilization, abnormal swimming	Moderately toxic	156044/ Acceptable
Fathead minnow (*Pimephales promelas*), 0.37 g, 2.8 cm SL	*o*PP 99.25%	Static/ 7.2-7.7/ 76/ 16.8-17.3 ºC	96-h LC_{50} = 4.7 ppm ae 95% CI = 3.6-6.0 ppm ae Probit slope = NA NOAEC = 3.6 ppm ae, mortality	Moderately toxic	156044/ Acceptable
Fathead minnow (*Pimephales promelas*), 0.53 g, 3.4 cm SL	*o*PP 99.25%	Static/ 7.2-7.9/ 76/ 17.1-17.4 ºC	96-h LC_{50} = 5.5 ppm ae 95% CI = 4.7-6.6 ppm ae Probit slope = NA NOAEC = 5.1 ppm ae, mortality	Moderately toxic	156044/ Acceptable

CI = confidence interval; NA: Not applicable; N.R. = Not reported; SL = standard length; TN = test number; ts = test substance not corrected for percent a.i.

Freshwater Invertebrates

The available acute toxicity studies for the waterflea categorize *o*PP and salts as being moderately toxic to freshwater invertebrates (Table 20). The guideline (850.1010) for acute toxicity testing is satisfied. Chronic data (daphnid life-cycle, 850.1300) are expected to be required.

Table 20 – Freshwater Invertebrate Toxicity Data

Test Species	Test Material (% a.i.)	Exposure Type/ pH/ hardness[28]/ temperature	Toxicity Endpoint[30]	Toxicity Category	MRID/ Study Classification/ Comments
Waterflea (*Daphnia magna*), <24 hours old	Na-*o*PP·$4H_2O$ (97)	Static/ / / 25 ºC (room)	48-h EC_{50} = 2.4 ppm ae (3.8 ppm ts) 95% CI = 2.0-3.0 ppm ae (3.1 – 4.6 ppm ts)	Moderately toxic	110222/ Acceptable
Waterflea (*Daphnia magna*), <24 hours old	*o*PP (99.2)	Static/ 7.9-8.1/ 148/ 19.7-21.0 ºC	48-h EC_{50} = 2.51 ppm ae 95% CI = 1.5-3.9 ppm ae NOAEC = 0.78 ppm ae	Moderately toxic	156044/ Acceptable

CI = confidence interval; NA: Not applicable; N.R. = Not reported; SL = standard length; TN = test number; ts = test substance not corrected for percent a.i.

Estuarine/Marine Fish and Invertebrates

Two acute toxicity studies are available for invertebrates, but no data are available for fish. *Ortho*-phenyl phenol and salts are moderately to highly toxic to estuarine/marine invertebrates (Table 21). The guideline (850.1035, 850.1025 or 1055) for acute toxicity testing with estuarine/marine invertebrates is satisfied. Acute toxicity data (850.1075) are expected to be

[30] For *o*PP mg a.i. is equal to mg ae, whereas mg a.i. of the tetrahydrate sodium salt (Na-*o*PP·$4H_2O$) were converted to mg ae by multiplying by the molar weight ratio of *o*PP to Na-*o*PP·$4H_2O$ (170.2/264.28 = 0.664).

required for fish. Chronic data are expected to be required for fish (early life-stage, 850.1400) and an invertebrate (mysid life-cycle, 850.1350).

Table 21 – Estuarine/Marine Fish and Invertebrate Toxicity Data

Test Species	Test Material (% a.i.)	Exposure Type/ pH/ salinity[31]/ temperature	Toxicity Endpoint[31]	Toxicity Category	MRID/ Study Classification/ Comments
Sheepshead minnow (*Cyprinodon variegatus*)	Na-*o*PP	Flow-through	--	--	46751208/ Unacceptable Percent recoveries were below acceptable range
Mysid shrimp (*Americamysis bahia*), 5-6 days old[32]	Na-*o*PP (71.48[33])	Flow-through/ 8.1-8.3/19-22 ppt/ 19-26 ºC	96-h LC_{50} = 0.28 ppm ae (0.32 ppm a.i.) 95% CI: 0.23-0.37 ppm ae (0.26-0.42 ppm a.i.) 96-h NOAEC = 0.063 ppm ae (0.071 ppm a.i.) Mean measured	Highly toxic	46751203/ Acceptable
Eastern oyster (*Crassostrea virginica*) shell deposition, 43 $\pm$ 3.4 mm valve height	Na-*o*PP (71.48[33])	Flow-through/ 7.9 -8.1/ 30-32 ppt/ 20-23 ºC	96-h IC_{50} = 3.44 ppm ae (3.89 ppm a.i.) 95% CI = 2.76-3.67 ppm ae (3.12-4.15 ppm a.i.) 96-h NOAEC = 0.80 ppm ae (0.88 ppm a.i.)	Moderately toxic	46751202/ Acceptable
Quahog clam (*Mercenaria mercenaria*), 2-cell embryo	Na-*o*PP (75.9[34])	Static	48-h IC_{50} = >8.86 ppm ae (>10 ppm a.i.)	---	25816, 5002007/ Supplemental/ Mollusc guidelines not in existence at time of study. Unknown test temperature and water quality. A solvent control was not included but solvents were tested.
Quahog clam (*Mercenaria mercenaria*), 2 day old larvae	Na-*o*PP (75.9[34])	Static	10-d IC_{50} = 0.66 ppm ae (0.75 ppm a.i.) (survival and length)	Highly toxic	

CI = confidence interval; NA: Not applicable; N.R. = Not reported; SL = standard length; TN = test number; ts = test substance not corrected for percent a.i.

Aquatic Plants

Five aquatic plant studies are available to establish the toxicity of *o*PP and salts to vascular and non-vascular aquatic plants (Table 22). The guidelines for testing three algal species (850.4500)

[31] For *o*PP mg a.i. is equal to mg acid equivalent (ae), whereas mg a.i. of Na-*o*PP were converted to mg ae by multiplying by the molar weight ratio of *o*PP to Na-*o*PP (170.2/192.19 = 0.886).

[32] Range finding was conducted with < 24 hour old and 5-6 day old mysids, no difference in sensitivity was observed in the range-finding between these age classes.

[33] The test substance is actually Na-*o*PP·$4H_2O$ but is represented in the table as Na-*o*PP without the weight percent of water. With the weight percent of water added the purity of the test substance Na-*o*PP·$4H_2O$ is 98.16%.

[34] The test substance is actually Na-*o*PP·$4H_2O$ but is represented in the table as Na-*o*PP without the weight percent of water. With the weight percent of water added the purity of the test substance Na-*o*PP·$4H_2O$ is >99%.

and cyanobacteria (850.4550) are satisfied. Guideline 850.4400 for testing a vascular aquatic plant is not satisfied (the submitted study did not adhere to dosing progression standards). Data from this study and the non-vascular plant studies are expected to be sufficient to conduct the risk assessment and a new study is not expected to be required at this time.

Table 22 – Aquatic Plants Toxicity Data

Test Species	Test Material (% a.i.)	Exposure Type/ pH/ temperature	Toxicity Endpoint[31]	MRID/ Study Classification/ Comments
Duckweed (*Lemna gibba*)	Na-*o*PP (71.48[33])	Static renewal days 3 & 5/ 7.8-8.0 new, 8.4-9.4 aged / 24 °C	7-day IC_{50} = 5.5 ppm ae (6.2 ppm a.i.) 7-day IC_{05} [35] = 0.63 ppm ae (0.71 ppm a.i.) Mean measured concentrations	46751209/ Supplemental[36]
Green algae (*Selenastrum capricornutum*)	*o*PP (99.91)	Static/ 7.41-8.90/ 24±2 °C	96-h IC_{50} = 1.39 ppm ae 96-h NOAEC = 0.42 ppm ae Mean measured concentrations	45688201/ Acceptable
Blue-Green alga (*Anabaena flos-aquae*)	Na-*o*PP (71.48[33])	Static/ 6.8-7.8/ 24±2 °C	96-h IC_{50} = 2.0 ppm ae (2.3 ppm a.i.) 96-h NOAEC = 0.030 ppm ae (0.034 ppm a.i.)	46823801/ Supplemental/ 4X dose progression, age of medium, reduced PAR
Freshwater diatom (*Navicula pelliculosa*)		Static/ 7.2-9.4/ 24±2 °C/	96-h IC_{50} = 1.7 ppm ae (1.9 ppm a.i.) 96-h NOAEC = 0.52 ppm ae (0.59 ppm a.i.)	46751205/ Acceptable
Marine diatom (*Skeletonema costatum*)			96-h IC_{50} = 5.7 ppm ae (6.4 ppm a.i.) 96-h NOAEC = 2.1 ppm ae (2.4 ppm a.i.)	46751201/ Acceptable

NA = Not applicable; N.R. = Not reported; ppt: parts per thousand; PAR = Photosynthetically active radiation

Emergent Rooted Aquatic Macrophytes

The available studies testing rice *(Oryza sativa)* are presented in Table 23. Inhibition of emergence and growth in rice was 7% and 5%, respectively, in Tier I tests. The guideline requirements (850.4225, 850.4250) are satisfied for Tier I testing. Tier II testing is not required, because inhibition in emergence and growth was less than 25% in the Tier I tests.

Table 23 – Emergent Rooted Aquatic Plant Toxicity Data

Test Species	Test Material (% a.i.)	Toxicity Endpoint[31]	MRID/ Study Classification/ Comments
Rice (*Oryza sativa*) – seedling emergence (Tier I)	Na-*o*PP (71.48[33])	IC_{25} >886 ppm ae (>1000 mg a.i./L) NOAEC = 886 ppm ae (<1000 mg a.i./L) 7% emergence inhibition after 14 days (1000 mg a.i./L)	46751207 Acceptable
Rice – vegetative vigor (Tier I)		IC_{25} >886 ppm ae (>1000 mg a.i./L) NOAEC = 886 ppm ae (<1000 mg a.i./L) 2% inhibition in dry weight after 14 days (1000 mg a.i./L)	46751204 Acceptable

[35] Where a NOAEC cannot be calculated, an IC_{05} will be used as a surrogate. Because of the problems with the IC_{50} being lower than the LOAEC, the hypothesis method was deemed problematic and the IC_{05} used rather than asking for a repeat of the study.

[36] Dosing progression did not adhere to guideline standards (e.g., doses separated by a dilution factor of 4-5X instead of recommended 2X); results in this study occurred between highest and second highest treatment levels, making the IC_{50} lower than the LOAEC.

Terrestrial Plants

Seedling emergence and vegetative vigor data are expected to be required (with the exception of data for rice).

Sediment-dwellers

No data are available. Chronic toxicity data (no guideline number) are expected to be required for sediment-dwelling freshwater (2 species) and estuarine/marine (1 specie) invertebrates, because *o*PP and salts are expected to sorb to soil and persist (i.e., half-life $\geq$10 days) in aquatic sediments.

Appendix C References

MRID 46010: Levenstein, I. (1964) To Observe the Effects of Lysol Spray Disinfectant When Sprayed Directly upon or in the Vicinity of Parakeets: Assay No. 46229. (Unpublished study received Aug 27, 1969 under 777-20; prepared by Leberco Laboratories, submitted by Lehn & Fink Products Corp., Montvale, N.J.; CDL: 100493-B).

MRID 51597: McCann, J.A. (1974) Letter sent to Charles College dated Oct 22, 1974 Fish toxicity data. (U.S. Environmental Protection Agency, Animal Biology Laboratory, unpublished study; CDL:224700-T).

MRID 110135: Pitcher, F. (1973) Dowicide A: Bluegill: Test No. 640. (U.S. Environmental Protection Agency, Pesticides Regulation Div., Animal Biology Laboratory; unpublished study; CDL:129165-A).

MRID 110137: McCann, J. (1972) Nalco D-2303: Bluegill: Test No. 434. (U.S. Agricultural Research Service, Pesticides Regulation Div., Animal Biology Laboratory; unpublished study; CDL:129754-A).

MRID 110171: WARF Institute, Inc. (1970) Report: WARF No. 9110671. (Unpublished study received Apr 21, 1970 under 5590-106; submitted by ATI Research Center, Milford, CT; CDL:223189-B).

MRID 110203: McCann, J. (1974) Letter sent to C. College dated Oct 22, 1974 Toxicity of Dowicide A to fish. (U.S. Environmental Protection Agency, Animal Biology Laboratory; unpublished study; CDL: 223721-A).

MRID 110222: Batchelder, T.; McCarty, W. (1977) Toxicity of Dowicide A to Daphnids: ES-154. (Unpublished study received Oct 28, 1977 under 464-78; submitted by Dow Chemical U.S.A., Midland, MI; CDL: 232113-A).

MRID 110232: Bentley, R. (1975) Acute Toxicity of Dowicide CO to Bluegill and Rainbow Trout: GH-RC 62. (Unpublished study received Aug 25, 1976 under 464-126; prepared by Bionomics, EG & G Environmental Consultants, submitted by Dow Chemical U.S.A., Midland, MI; CDL:233706-A).MRID 118876: Vis-Ko, Inc. (1970) Effects of Dowicide 1 on Minnows. (Unpublished study received Mar 11, 1971 under 1773-8; CDL:006636-A).

MRID 137908: Dow Chemical U.S.A. (19??) Fish, Snail and Daphnia Toxicity of Torsite M-2469-X-200. (Unpublished study received Sep 25, 1964 under unknown admin. no.; CDL:110833-C).

MRID 156044: Dill, D.; Milazzo, D.; Bartlett, E.; *et al*. (1985) Evaluation of the Toxicity of Dowicide 1 Antimicrobial, Technical *O*-Phenylphenol, to Representative Aquatic Organisms: ES-811. Unpublished study prepared by Dow Chemical U S A. 17 p.

MRID 160149: Grimes, J. (1986) *Ortho*-phenylphenol Technical: A Dietary LC_{50} Study with the Bobwhite: Final Report: Project No. 103-246. Unpublished study prepared by Wildlife International Ltd. 17 p.

MRID 160150: Grimes, J. (1986) *Ortho*-phenylphenol Technical: An Acute Oral Toxicity Study with the Mallard: Final Report: Project No. 103-248. Unpublished study prepared by Wildlife International Ltd. 18 p.

MRID 160151: Grimes, J. (1986) Ortho-phenylphenol Technical: A Dietary LC_{50} Study with the Mallard: Final Report: Project No. 103-247. Un- published study prepared by Wildlife International Ltd. 18 p.

MRID 164770: Vis Co, Inc. (1971) Effects of Dowicide 1 on Minnows and Determination of Fish Toxicity. Unpublished compilation. 4 p.

MRID 42500204: Campbell, S.; Jaber, M. (1992) Sodium O-Phenylphenate (Dowicide A): An Acute Oral Toxicity Study with the Northern Bobwhite: Lab Project Number: ES-DR-0000-9198-6: ES-25-42: 103-383. Unpublished study prepared by Wildlife Int'l Ltd. 25 p.

MRID 42500206: Campbell, S.; Jaber, M. (1992) Sodium O-Phenylphenate (Dowicide A): A Dietary LC50 Study with the Mallard: Lab Project Number: 103-382. Unpublished study prepared by Wildlife Int'l Ltd. 21 p.

MRID 45688201: Hicks, S. (2002) *Ortho*-Phenyl Phenol: Growth Inhibition Test with the Green Alga, *Selenastrum capricornutum*: Lab Project Number: 46980: 010167. Unpublished study prepared by ABC Laboratories, Inc. 55 p. {OPPTS 850.5400}.
MRID 46751201: Hoberg, J. (2006) OPP/SOPP - Acute Toxicity to the Marine Diatom, Skeletonema costatum, Under Static Conditions. Project Number: 12550/6389, 050375. Unpublished study prepared by Springborn Smithers Laboratories. 68 p.
MRID 46751202: Cafarella, M. (2006) OPP/SOPP - Acute Toxicity to Eastern Oyster (*Crassostrea virginica*) Under Flow-Through Conditions. Project Number: 12550/6382, 050368. Unpublished study prepared by Springborn Smithers Laboratories. 60 p.
MRID 46751204: Teixeira, D. (2006) OPP/SOPP - Determination of Effects on Vegetative Vigor of Rice (Oryza sativa). Project Number: 12550/6385, 050371. Unpublished study prepared by Springborn Smithers Laboratories. 61 p.
MRID 46751205: Hoberg, J. (2006) OPP/SOPP - Acute Toxicity to the Freshwater Diatom (Navicula pelliculosa). Project Number: 12550/6388, 050374. Unpublished study prepared by Springborn Smithers Laboratories. 63 p.
MRID 46751207: Teixeira, D. (2006) OPP/SOPP - Determination of Effects on Seedling Emergence of Rice (Oryza sativa). Project Number: 12550/6384, 050370. Unpublished study prepared by Springborn Smithers Laboratories. 60 p.
MRID 46751208: Hoberg, J. (2006) OPP/SOPP - Acute Toxicity to Sheepshead Minnow (*Cyprinodon variegatus*) under Flow-through Conditions. Project Number: 12550/6381, 050367. Unpublished study prepared by Springborn Smithers Laboratories. 56 p.
MRID 46751210: Hoberg, J. (2006) OPP/SOPP - Toxicity to Bluegill Sunfish (Lepomis macrochirus) Under Flow-Through Conditions: (Dowicide A Antimicrobial). Project Number: 12550/6391, 050412. Unpublished study prepared by Springborn Smithers Laboratories. 57 p.
MRID 46751203: Hoberg, J. (2006) OPP/SOPP - Acute Toxicity to Mysids (*Americamysis bahia*) Under Flow - Through Conditions. Project Number: 12550/6383, 050369. Unpublished study prepared by Springborn Smithers Laboratories. 61 p.
MRID 46751206: Hoberg, J. (2006) OPP/SOPP - Acute Toxicity to Rainbow Trout (*Oncorhynchus mykiss*) Under Flow-Through Conditions. Project Number: 12550/6390, 050411. Unpublished study prepared by Springborn Smithers Laboratories. 56 p.
MRID 46823801: Hoberg, J. (2006) OPP/SOPP - Growth Inhibition Test with Freshwater Blue-Green Alga (*Anabaena flos-aquae*). Project Number: 12550/6387, 050373. Unpublished study prepared by Springborn Smithers Laboratories. 66 p.
MRID 48135402: Caspers, N. (2010) OSRI Rationale: *Ortho*-Phenylphenol: EDSP Order Numbers: EDSP-064103-225, EDSP-064103-226: Life Cycle Test with Water Fleas -- *Daphnia magna*. Project Number: 51/A/88. Unpublished study prepared by Bayer AG. 43 p.
MRID 48135403: Caspers, N. (2010) OSRI Rationale: *Ortho*-Phenylphenol: EDSP Order Numbers: EDSP-064103-225, EDSP-064103-226: Preventol O Extra: *Daphnia magna* Reproduction Test. Project Number: 1092/A/01/DL. Unpublished study prepared by Bayer AG. 24 p.
MRID 48135404: Caunter, J.; Williams, T. (2002) OSRI Rationale: Ortho-Phenylphenol: EDSP Order Numbers: EDSP-064103-225, EDSP-064103-226: Preventol O Extra: Determination of Effects on the Reproduction of Fathead Minnow (Pimephales promelas). Project Number: AH0603A, 07950/2000, BL7213/B. Unpublished study prepared by AstraZeneca UK, Ltd. 62 p.
MRID 48672606: Lehman, C. ; Fiting, J. ; Hutchinson, K. ; et al. (2012) *Ortho*-PhenylPhenol: The Fish Short-Term Reproduction Assay Using the Fathead Minnow, *Pimephales promelas*. Project Number: 111032. Unpublished study prepared by The Dow Chemical Co. 147p.
MRID 48672607: Lehman, C.; Hutchinson, K.; Fiting, J.; et al. (2011) *Ortho*-PhenylPhenol: The Amphibian Metamorphosis Assay Using the African Clawed Frog, *Xenopus laevis*. Project Number: 111018. Unpublished study prepared by The Dow Chemical Co. 202p.
MRID 48916901: Lehman, C.; Hutchinson, K.; Fiting, J. et al. (2012) *Ortho*-Phenylphenol: The Amphibian Metamorphosis Assay Using the African Clawed Frog, *Xenopus laevis*. Project Number: 111018. Unpublished study prepared by The Dow Chemical Company. 204p.

Appendix D Screening Level Down-the-Drain Analysis

The Down-the-Drain (DtD) module of E-FAST (Exposure and Fate Assessment Screening Tool), version 2, was used to screen for the potential for aquatic organisms downstream of domestic wastewater treatment plants to be exposed to *o*PP and salts and/or their degradates. The DtD module uses daily per capita release of household wastewaters, stream dilution factors, and wastewater treatment plant removal efficiency to provide both high-end and median (average) time-averaged surface water concentrations of chemicals discharged from domestic wastewater treatment plants. The high-end scenario uses surface water concentrations downstream of domestic wastewater treatment plants based on the 10^{th} percentile stream dilution factor (SDF); the average scenario uses surface water concentrations based on the 50^{th} percentile SDF. SDF is defined as the ratio of the stream flow downstream of a wastewater treatment plant to the wastewater treatment plant flow. Inputs used to run the DtD module included concentrations of concern (COCs) for aquatic organisms, percent removal during wastewater treatment, and wastewater treatment plant (WWTP) influent volumes. Wastewater treatment plant influent volumes are often derived from information on maximum annual production volume or consumption volume of the chemical being assessed. Sometimes hypothetical WWTP influent volumes are used to estimate potential exposures to give an idea of how much influent volume would be needed to trigger a potential concern.

The results of the DtD module are expressed as number of days of exceedance of COCs for aquatic organisms. COCs for acute effects were determined by dividing LC_{50} values from acute toxicity tests on aquatic vertebrates and invertebrates by 2. COCs for chronic effects for non-listed species were based on No Observed Adverse Effects Concentration (NOAEC) values from tests on aquatic vertebrates and invertebrates. COCs for listed endangered and threatened aquatic organisms were determined by dividing LC_{50} values from acute toxicity tests on aquatic vertebrates and invertebrates by 20. Acute COCs for aquatic vascular plants and algae are based on EC_{50} values. COCs for endangered algae and aquatic vascular plants are based on NOAEC values.

The DtD module was run using a high-end scenario to estimate exceedances of concentrations of concern for aquatic organisms.

Appendix E Product Chemistry

Ortho Phenyl Phenol and Salts product chemistry information is summarized in Table 4 and Table 24 (source: MRIDs 101697, 41914901, 41605001, 41609501, 41609502, 41609503, 41609504, 41609505, 42097001, 42381901, 42441701, 42441702, 42441703, 42441704, 42457001, 42500201, 42500202, 42528701, 43994201 and EPI Suite v4.1).

Table 24 – Product Chemistry of *o*PP and Salts

OPPTS Guideline No.	Physical and Chemical Properties	***o*PP**	**Na-*o*PP**	K-*o*PP
830.1550	Product identity and composition	Refer to Table 3.	Refer to Table 3.	Refer to Table 3.
830.1600	Description of materials used to produce the product	Confidential Business Information (CBI)	CBI	CBI
830.1620	Description of production process	CBI	CBI	CBI
830.1650	Description of Formulation Process	CBI	CBI	CBI
830.1670	Discussion of Formation of Impurities	CBI	CBI	CBI
830.1700	Preliminary analysis	CBI	CBI	CBI
830.1750	Certified limits	CBI	CBI	CBI
830.1800	Enforcement analytical method	Gas Chromatography (GC)	GC	GC
830.1900	Submittal of samples	CBI	CBI	CBI
830.6302	Color	White to light buff crystals	White crystalline flakes	White flakes
830.6303	Physical State	Solid (flakes)	Solid (flakes)	Solid (flakes)
830.6304	Odor	Slight phenolic odor	Slight phenolic odor	Slight phenolic odor
830.6313	Stability to normal and elevated temperatures, metals, and metal ions	Stable at normal conditions.	Stable at normal conditions.	Stable at normal conditions.
830.7000	pH	6.1 in aqueous solution at 22.7 ° C	12 to 13.5 in saturated water solution at 25° C.	12 to 13.5 in saturated water solution at 25° C.
830.7050	UV/Visible Absorption	245 to 287nm Not expected to absorb UV at $\lambda > 300$ nm	-------	-------
830.7200	Melting point	56-58 °C.	230.07 °C (Source: EPI Suite)	230.07 °C (Source: EPI Suite)
830.7220	Boiling point	286°C at 760 mm Hg	537.41 °C (Source: EPI Suite v4.1)	537.41 °C (Source: EPI Suite v4.1)
830.7300	Density	1.213 g/cu cm at 25° C.	1.3 g/cu cm at 25° C.	1.3 g/cu cm at 25° C.
830.7370	Dissociation Constants in water	pKa = 9.55 at 22.5°C. pKa = 9.9 at 25°C. pKa = 9.97 at 25°C. It is a weak acid.	Dissociates in water. pKa: 9.84 at 20ºC.	Dissociates in water. pKa: 9.84 at 20ºC.
830.7520	Particle size, fiber length, & diameter distribution	Not Applicable; soluble in water	Not Applicable; soluble in water	Not Applicable; soluble in water

OPPTS Guideline No.	**Physical and Chemical Properties**	***o*PP**	**Na-*o*PP**	K-*o*PP
830.7550	Partition coefficient (*n*-octanol/water) Log *K*ow	3.3 (Source: EPI Suite v4.1) log Pow: 3.09-3.36 log Pow: 3.12 (20 °C, pH 7).	0.59 (Source: EPI Suite v4.1).	0.59 (Source: EPI Suite v4.1).
830.7840	Water Solubility	700 mg/L at 25°C in water. 0.760 g/1000 g in water (pH 5.67) (20ºC).	60.6 g/100 mL, 53.37% (w/w) (20ºC). 534 g/1000 g in water (pH 13.61) (20ºC).	Highly water soluble. 534 g/1000 g in water (pH 13.61) (20ºC).
830.7950	Vapor pressure	2.00 x 10^{-3} mm Hg at 25° C (Source: EPI Suite version 4.1, Experimental). 1.6 x 10^{-3} mm Hg at 25ºC. 0.0017 mmHg at 25ºC.	1.91 x 10^{-11} mm Hg at 25 °C (Source: EPI Suite v4.1). 1.8 x 10^{-9} mmHg at 25ºC.	1.91 x 10^{-11} mm Hg at 25 °C (Source: EPI Suite v4.1).

Appendix F Comments Received Concerning the Preliminary Work Plan

On September 25, 2013 EPA opened a 60-day public comment period on the preliminary work plan (PWP) for the registration review of for *ortho*-Phenyl Phenol and Salts. The comment period ended on November 25, 2013. During the public comment period the Agency received two submissions from:

- The FIFRA Endangered Species Task Force (FESTF), and
- The Physicians Committee for Responsible Medicine (PCRM)

Submitter: PCRM

1. **Comment:** We recommend that OECD Test Guideline 223, Avian Acute Oral Toxicity Test, be used as the protocol instead of EPA Guideline 850.2100 in the interest of reducing the numbers of animals used by up to 61%.[37] We also refer the registrant to the "Guidance for Classifying Studies Conducted Using the OECD Test Guideline 223 (TG223) (Acute Avian Oral Sequential Dose Study)" available on the Agency's website.

   Response: The Agency concurs that the "Guidance for Classifying Studies Conducted Using the OECD Test Guideline 223 (TG223) (Acute Avian Oral Sequential Dose Study)" should be consulted if the registrant intends to submit an avian acute oral study based on OECD Test Guideline 223. The guidance can be found at: http://www.epa.gov/pesticides/science/efed/policy_guidance/team_authors/terrestrial_biology_tech_team/review_avian_acute_oral_oecd_tg223.htm.
   It should be noted that the guidance specifies that "a study conducted using TG223 may be classified as "acceptable" (*i.e.*, adequate for use in risk assessment and fulfills a data requirement for avian acute oral toxicity data) if it is scientifically valid, is conducted using the "LD_{50}- slope test" or "limit dose test" guidelines (the "LD_{50} - only test" is not adequate for fulfilling data requirements) (see APPENDIX A for details), **and meets all of the following criteria**:

   - The study is conducted using bobwhite quail (other test species may be acceptable if they have low background mortality in the laboratory and do not regurgitate during the study; however, if a species other than bobwhite quail is used, the study should be reviewed by the TBTT - see below; please note that the background mortality data for the species in question should be available from the submitting laboratory at the time of the TBTT review).
   - The chemical being tested does not cause delayed effects.

[37] OECD. (2010). Test Guideline 223: Avian Acute Oral Toxicity Test Method. OECD Guidelines for the Testing of Chemicals. Website accessed on August 31, 2012 at http://lysander.sourceoecd.org/vl=3006812/cl=16/nw=1/rpsv/ij/oecdjournals/1607310x/v1n2/s33/p1

- For a "limit dose test", it is conducted at 2,000 mg a.i./kg-bw or the environmentally relevant concentration (whichever is greater).
- For the "LD_{50} - slope test", the raw data and results are submitted electronically using the SEquential DEsign Calculator (SEDEC) (the Excel calculator that determines the placement of doses during testing and is used to estimate the LD_{50}, slope and confidence limits for TG223 studies) (see APPENDIX A for details).
- The study meets the same validity requirements as 850.2100 (*e.g.*, a study should be invalidated if > 10% of the controls die).
- Control birds are not added during the course of the study.

Studies that deviate from the above criteria may be classified as "acceptable" or "supplemental" if they are considered adequate for use in risk assessment or "invalid" if they are not scientifically sound; however, consultation with the TBTT will need to confirm the classification for any TG223 study that deviates from the above criteria. If you have questions regarding this policy you may contact any of the project workgroup members listed at the end of Appendix A to this guidance memo."

2. **Comment:** With respect to the immunotoxicity study we found the following two studies on Toxnet that may fulfill the Agency's needs without additional testing. Using such a weight-of-evidence approach, if possible, is consistent with Agency policy outlined in the Guiding Principles for Data Requirements document published on May 31, 2013.[38]
o-Phenylphenol does not induce changes in immune function in mice following short term oral administration. This finding was confirmed in studies in which B6C3F1 mice were administered oral doses of o-phenylphenol (up to 200 mg/kg day) for 10 days and then examined for a variety of immune functions.[39]
o-Phenylphenol was given with drinking water: 10, 100 ug/mL for 80 weeks to male and female BALB/c mice. On 80 weeks the spleen weights of the treated females were higher than in the control females. Treated female groups showed immunosuppression in the lymphocyte transforming test (LTT) and in the plaque forming assay (PFC). In the treated male groups there were no significant effects on immunoproerties.[40]

   Response: The Agency thanks PCRM for this information and will consider these studies as it conducts the registration review and makes its registration review decisions. EPA's issuance of a DCI is a public statement that the data is needed, and will be relied on, thus "triggering" the data compensation provisions of section 3(g)(2)(B) of FIFRA.

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[38] EPA OPP. Guiding Principles for Data Requirements http://www.epa.gov/pesticides/regulating/data-require-guide-principle.pdf

[39] DHHS/NTP; Toxicology and Carcinogenesis Studies of ortho-Phenylphenol alone and with 7,12-Dimethylbenz(a)anthracene in Swiss CD-1 Mice. (Dermal Studies) p.14 (1986) Technical Rpt Series No. 301 NIH Pub No. 86-2557.

[40] European Commission, ESIS; IUCLID Dataset, Biphenyl-2-ol (90-43-7) p.124 (2000 CD-ROM edition). Website accessed on November 20, 2013 at http://esis.jrc.ec.europa.eu/

Submitter: FIFRA Endangered Species Task Force

3. **Comment:** FESTF requests that any technical registrant for ortho-phenyl phenol who is not a member of the FESTF (or a company having met its data compensation obligations) be asked to provide a formal offer-to-pay to FESTF for reliance on their data. In their comment, FESTF also noted that Dow AgroSciences LLC is an FESTF member.

   Response: The Agency thanks the FESTF for its comment and will consider all appropriate information as it conducts the registration review and makes its registration review decisions.